EVALUATION OF A HYPOLIPIDAEMIC / CARDIOPROTECTIVE DRUG OF DABUR INDIA LIMITED IN TREATMENT OF HYPERLIPIDAEMIA

THESIS

For

DOCTOR OF MEDICINE

(MEDICINE)

BUNDELKHAND UNIVERSITY
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DINESH GUPTA

C E R T I F I C A T E

This is to certify that the work entitled "EVALUATION OF A HYPOLIPIDAEMIC/CARDIOPROTECTIVE DRUG OF DABUR INDIA LIMITED IN TREATMENT OF HYPERLIPIDAEMIA" which is being submitted as thesis for M.D.(Medicine) examination of Bundelkhand University, Jhansi, 1993 by DR. DINESH GUPTA has been carried out in the department of Medicine, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the department as per University regulations.

Dated: 20/7/92

(R. C. Arora)
M.D., D.Sc.,
Professor and Head,
Department of Medicine,
M.L.B. Medical College,
JHANSI.

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Dated: 20/7/92

Agarwal

(Navnit Agarwal)
M.D.,
Assistant Professor,
Department of Medicine,
M.L.B. Medical College,
Jhansi.

(GUIDE)

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(R. C. Arora)
M.D., D.Sc.,
Professor and Head,
Department of Medicine,
M.L.B. Medical College,
Jhansi.

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Dated: 20/7/92.

Sunita Arora

(Sunita Arora)
M.S.,
Associate Professor,
Department of Obstetrics, & Gynaecology,
M.L.B. Medical College,
Jhansi.

(CO-GUIDE)

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Dinesh Gupta

(Dinesh Gupta)

INTRODUCTION

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Ischaemic heart disease consists of major cause of mortality in present stress age and is a global problem involving both developing as well as developed countries (W.H.O., 1982; Hiroyasu et al, 1989; Gordon, 1977). Main risk factors of ischaemic heart disease are atherosclerosis and hyperlipidemia leading to deposition of lipids on the intima of arteries causing narrowing of vessels. Due to narrowing of vessels, specially coronary arteries, blood supply to heart becomes deficient resulting into myocardial ischaemia (Edwin, 1990; Lewis, 1988).

Relation of serum level of total cholesterol to coronary heart disease (or atherosclerotic heart disease) is well established (WHO, 1982; Atherosclerosis study group, 1984; Stamler, 1986; Conference on Health effects of blood lipids, 1979).

An increased risk of coronary heart disease (CHD) is associated with a high serum total cholesterol concentration (Gordon, 1977; Goldbourt, 1985; Grundy, 1986; 1987; Neaton, 1984; Thomas, 1990) and low density lipoprotein (LDL) cholesterol (Steinberg et al, 1989; Brown et al, 1986; Keys et al, 1972; Kannel et al, 1971), a low high density lipoprotein (HDL) (Castelli, 1986a; Goldbourt, 1985; Kannel et al, 1979) and in some circumstances high triglycerides (Castelli, 1986b).

Increased lipids:triglycarides, total cholesterol, LDL and very low density lipoprotein (VLDL) cholesterol and decreased HDL cholesterol are the major factors in causing atherosclerosis and ischaemic heart disease (IHD) (Bhatia, 1980).

The analysis of results of serum cholesterol levels and six year mortality from Stroke in 350, 977 men screened for the multiple risk factor intervention trial (MRFIT) showed that the rate of mortality due to coronary heart disease was 124.4 and 160.3 per 10,000 among the men aged 35-57 years with S. cholesterol levels more than 280 and 300 mg/dl respectively. This rate was highest in the study. It was also observed that within every cholesterol category age adjusted death rates from coronary heart disease were higher than for all strokes. Death rate from CHD and that from all cardiovascular diseases were positively associated with serum cholesterol levels(Hiroyasu et al, 1989).

Of particular clinical significance is the evidence that certain plasma lipoprotein abnormalities are casually related to atherosclerosis and atherosclerotic heart disease and others are predictive of a high risk of this disorder (Lewis, 1988). Elevation of serum cholesterol level or more specifically a low density lipoprotein(LDL) cholesterol level is widely accepted as a major risk factor for development of ischaemic heart disease (Key, 1972; Kannel et al, 1971).

Recent clinical and experimental studies of various kinds have firmly established that elevated plasma concentrations of LDL are associated with accelerated atherogenesis (Tyroler, 1987; Goldstein et al, 1977; Steinberg, 1983; 1989).

There is now good evidence from clinical trials and other observations that reduction of serum cholesterol in men with high concentrations can reduce the incidence of coronary heart disease (Consensus conference, 1985; Committee on medical aspects, 1984; Lipid Research Clinic, 1984a, 1984b). Clinical trials in selected patients seem to indicate that effective modification of risk factors (e.g. plasma lipid level) can slow the growth of coronary atherosclerosis (Edwin, 1990). Clinical intervention studies have demonstrated the therapeutic value of correcting hypercholesterolemia.(Tyroler, 1987; Lowering blood cholesterol, 1985).

Medical scientists are of the opinion that anti-lipidemic, antidiabetic and antihypertensive drugs and other measures that can decrease catecholamine levels are considered to be remedy for myocardial infarction (Raab, 1971). It is now a well established fact that reduction in blood cholesterol levels reduces the risk of myocardial ischemia. 25% reduction of blood cholesterol levels reduces the risk of myocardial ischaemia by 50% (lowering blood cholesterol 1985; Tyroler, 1987).

Vigorous global research is going on to search the agents to control hyperlipidemia. Indian scientists have directed their research towards herbs having hypolipidemic and cardioprotective potential based on few references in age old Ayurvedic texts.

The present formulation is based upon the thorough research data accumulated so far (Satyavati et al, 1966, 1969a; 1969b; 1987; Sastry, 1967; Saxena, 1980; Tripathi et al, 1968; 1975; 1976; 1979; 1984; Dwivedi et al, 1987; 1988; 1989). Hence it was felt desirable to conduct clinical trials on this new combination of age old hypolipidemic/cardioprotective herbal drugs, Terminalia arjuna W & A bark, Inula racemosa hook root and Commiphora mukul ex stocks resin with the primary aim of analyzing the effect of the drug on different components of serum lipids i.e. on total serum cholesterol, triglycerides, VLDL, LDL and HDL.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Cholesterol is a neutral derived lipid and is designated as 3-hydroxy-5, 6-cholestene. It is widely distributed in all cells of the body, but particularly in nervous tissue. It is the parent compound of all steroids synthesized in the body. It occurs in animal fats but not in plant fats. The greater part of cholesterol of the body arises by synthesis (about 1 g/day) whereas only about 0-3 g/day is provided by the average diet.

Cholesterol enters the body with chylomicrons. Triglycerides of chylomicrons are hydrolyzed and residual particles, called chylomicron remnants, are removed by the liver. The liver likewise secretes triglyceride rich lipoproteins called VLDL which are degraded into smaller VLDL remnants. This can be removed by the liver or converted to LDL. The LDLs are the major cholesterol carrying lipoproteins in plasma. The major pathway for removal of LDLs is via LDL receptors. It has been found that patients with familial hypercholesterolemia have defective LDL receptors on cells which means that they are unable to clear cholesterol, thus leading to high plasma cholesterol levels. There are receptors on cell membranes which control the uptake of LDL and hence cholesterol from plasma into cells. The activity of these LDL receptors is under feedback control. LDL is the carrier of cholesterol and is responsible for the delivery of

cholesterol to peripheral cells where the cholesterol can be used in cell membranes or for steroid hormone synthesis depending upon the tissue (Thomas, 1990).

Unfortunately, in our society the circulating levels of LDL cholesterol are so high in many people that they saturate this route and large quantities of cholesterol enter the cells by a second uncontrolled route. This cholesterol does not stop cells own synthesis of cholesterol nor does it influence the LDL receptors on the cells. The result of this is that the concentration of cholesterol in cells can rise to abnormally high values leading to development of atheroma (atherosclerosis) and eventually coronary heart disease (Thomas, 1990).

Hyperlipidemia is an important modifiable risk factor for atherosclerosis (Keys et al, 1958). Hyperlipidemias (hyperlipoproteinemias) are disturbance of lipid transport that result from accelerated synthesis or retarded degradation of lipoproteins that transport cholesterol and triglycerides through plasma (Edwin, 1990).

Hyperlipoproteinemias are traditionally defined as conditions in which the concentration of cholesterol or triglyceride carrying lipoproteins in plasma exceeds an arbitra normal limit, typically defined as ninety fifth percentile of a random population (Brown et al, 1990).

Several large surveys reveal a positive correlation between the concentration of plasma cholesterol and risk of CHD. There is no level of cholesterol below which coronary events are absent. But it has been shown by Framingham study and MRFIT that risk of CAD rises beyond serum cholesterol of 180 mg/dl. A long term prospective study in our population to assess the relation of serum lipids and CAD is lacking. We will have to go therefore, by the recommendations of NCEP which desires the level of total cholesterol to be below 200 mg/dl and that of LDL-c below 130 mg/dl.

TYPES OF HYPERLIPIDEMIAS

It has been classified following two approaches. One approach is related to clinical, genetic and metabolic entities (Lewis, 1988; Brown et al, 1990; MEdwin,1990) (Table 1, 2) while the other is based on the pattern of lipoprotein abnormalities(Fredericksom et al/WHO,1988) (Table 3).

As evident in table 1 & 2 hyperlipoproteinemias can be designated as either primary or secondary. Secondary hyperlipoproteinemias are complications of more generalised metabolic disturbances such as diabetes mellitus, hypothyroidism and excess intake of alcohol. The primary hyperlipoproteinemias can be divided into two major groups : those caused by an inherited single gene defect (monogenic hyperlipoproteinemias) and those that appear to be caused by a combination of multiple subtle genetic factors that act together with environmental insults(multifactorial or polygenic lipoproteinemias).

TABLE 1 : PRIMARY HYPERLIPIDEMIAS.

Disease	Primary Disorder	Kinetic disorder	Plasma cholesterol	Plasma Triglyceride	Lipoprotein in excess	WHO Type	Atherosclerosis risk
Familial Hypercholesterolemia	Low receptor defects	Impaired LDL catabolism and LDL overproduction	+++	Normal, +	IDL	IIa, IIb	+++
Familial combined hyperlipidemia	-	Overproduction of LDL & VLDL	+	+	LDL, VLDL	IIa, IIb IV	++
Familial Hyper triglyceridemia	-	Impaired catabolism of VLDL triglyceride and Apo B, with over production of VLDL triglyceride	+	+++	VLDL, CM	V, IV	?
Chylomicronaemia	Lipoprotein lipase deficiency or Apo C-II deficiency or circulating lipoprotein lipase inhibitor.	Impaired clearance of chylomicrons	+	+++	CM, VLDL	I, V	-
Remnant hyper lipoproteinemia	Abnormal Apo E and other genetic or acquired disorders	Impaired remnant particle catabolism reduced conversion to LDL, with or without IDL over production.	++	++	IDL, CM Remnants	III	++
Common hyper cholesterolemia	-	LDL overproduction	+	Normal	LDL	IIa	+

TABLE 2 : SECONDARY HYPERLIPIDEMIAS.

Disease	Hyper-cholesterolemia	Hyper-Triglyceridemia	Plasma lipoprotein elevation CM	IDL	VLDL	LDL	WHO type	Mechanism of hyperlipidemia
Diabetes Mellitus	-	+	+	-	+++	=	IV	Increased secretion of VLDL decreased catabolism of VLDL & Chylomicrons due to reduced lipoprotein lipase activity.
Hypothyroidism	+	-	-	+	-	+++	IIa	Decreased catabolism of VLDL & IDL
Nephrotic syndrome	+	+	-	-	++	+++	IIa or IIb	Increased secretion of VLDL. Direct secretion of LDL from Liver. Decreased catabolism of VLDL & LDL.
Acute hepatitis	+	-	-	-	+++	-	IV	Decreased hepatic secretion of lecithin.
Renal failure	-	+	-	-	+++	-	IV	Decreased catabolism of VLDL due to reduced lipoprotein lipase activity.
Glycogen Storage disease	-	+	+	-	+++	-	IV	Increased secretion of VLDL, Decreased catabolism of VLDL and chylomicrons due to reduced lipoprotein lipase activity.
Growth hormone deficiency.	+	-	-	-	++	++	IIb	Increased secretion of VLDL with conversion to LDL.

Table continued .....

table continued ..

Anorexia nervosa.	+	-	-	-	-	++	IIa	Reduced biliary excretion of cholesterols and bile acids.
Acute porphyria	+	-	-	-	-	++	IIa	Unknown
Alcohol	-	+	+	-	+++	-	IV	Increased secretion of VLDL.
Oral contra-ceptives	-	+	+	-	+++	-	IV	Increased secretion of VLDL.
Corticosteroids	+	-	-	-	+	++	IIa or IIb	Increased secretion of VLDL with conversion to LDL.

TABLE 3 : TYPES OF HYPERLIPIDEMIA.

Type	Chylo-microns	VLDL	Remnants	LDL	Plasma cholesterol	Plasma Triglycerides
I	++	N	N	Low	+	+++
IIa	-	N	N	++	++	N
IIb	-	++	N +	++	++	++
III	+	+	++	Low	++	++
IV	-	++	N	N	+	++
V	++	++	N	Low	+	++

Classification of Frederickson, Levy and Lees (1988) extended by a world Health Organisation (WHO) committee. Frederickson, Levy and Lees (1988)/ World Healthn Organisation Committee Classification.

SEQUELAE OF HYPERLIPIDEMIA

Abnormalities of plasma lipid transport are associated with a wide clinical spectrum from silent aberrations of plasma lipoprotein concentration to grave disorders including life limiting cardiovascular, abdominal or neurological manifestation. Of particular clinical significance is the evidence that certain plasma lipoprotein abnormalities are casually related to atherosclerotic/ischaemic heart disease and others are predictive of a high risk of this disorder (Lewis, 1988; Kannel et al,1979). Elevated plasma lipoproteins are important clinically because they can cause two life threatening diseases, atherosclerosis and pancreatitis (Brown et al, 1987). Atherosclerosis has dual sequelae as thrombosis and infarction (Brown et al, 1990).

There is striking analogy between serum cholesterol and blood pressure on the epidemiological basis for identifying a large segment of population (10-15%) for intensive treatment (Martin et al, 1986).

The earlier attempts to investigate the biochemical nature of the atherosclerotic lesion incriminated cholesterol (Vogel, 1847; Windaus, 1910). Modern investigations continue to show cholesterol, particularly cholesterol esters, as the principal lipid ingredient of the atherosclerotic lesion (Smith, 1965; Insull et al, 1966; Bottcher et al, 1960). From the very beginning animal experiments designed to produce the induction of hypercholesterolemia

by one or the other means (Anitschkow et al, 1913; Wacher et al, 1913; Strong, 1976; Gresham, 1976).

Epidemiologic studies of the evolution of cardiovascular disease in human populations have for many years emphasized the importance of serum total cholesterol as a precursor of coronary heart disease (McGee et al, 1976; Intersociety commission for heart disease resources, 1970; Kannel et al, 1971; Carlson et al, 1972; Gordon et al,1974; Keys, 1970; Wilhelmsen et al, 1973; Westlund et al, 1972 and Rosemann et al, 1967). As a result of the great amount of researches conducted into the transport and intermediary metabolism of blood lipids during the past two decades attention has been focussed on the partition of the serum total cholesterol in the various lipoprotein fractions (Gofman et al, 1966; Fredrickson et al, 1967) and the atherogenic potential of each of the latter.

Epidemiological studies initially focussed almost exclusively on the serum total cholesterol showing a powerful relation of this lipid to the subsequent development of coronary heart disease (Key et al, 1958; Bronte-Stewart et al, 1955; Doyle et al, 1957; Chapman et al, 1957; Paul et al, 1963; Stamler et al, 1960 and Key et al, 1963).

Atherosclerosis, a sequel of hyperlipidemia, is a patchy nodular type of arteriosclerosis. The lesions commonly classified as fatty streaks, fibrous plaques and complicated lesions. They are characterised by an accumulation of lipid-filled smooth muscle cells and macrophages

(foam cells) and fibrous tissue in focal areas of the intima. There is a relation between fatty streaks and fibrous atherosclerotic plaques. In the coronary arteries, the extent of fatty streaks may be better indicator of clinically significant raised lesions later in life.Fibrous plaques, also called raised lesions or pearly plaques, are palpably elevated areas of intimal thickening and represent the most characteristic lesion of advancing atherosclerosis. The plaque is much thicker than the normal intima. Although the lipid, like that of fatty streaks, is mainly cholesterol ester, the principal esterified fatty acid is linoleic rather than oleic. Thus plaque cholesterol ester composition differs from fatty streaks but resembles plasma lipoproteins. The complicated lesion is a calcified plaque containing various degrees of necrosis, thrombosis and ulceration. With increasing necrosis and accumulation of gruel the arterial wall progressively weakens, and rupture of the intima can occur causing aneurysm and haemorrhage. Arterial embolism form when fragments of plaque dislodge into lumen. Stenosis and impaired organ function result from gradual occlusion as plaque thicken and thrombi form (Edwin, 1987).

Although the term generalised atherosclerosis is commonly used clinically, lesions are actually irregularly distributed ; different vessels are involved at different ages and to varying degrees (Edwin, 1987).

In the coronary arteries, raised lesions are most prominent in the main stem, the highest incidence being a short distance beyond the ostia.

Atherosclerosis is nearly always found in the epicardial (extramural) portions of the vessel, while the intramural coronary arteries are spared. Coronary atherosclerosis is often diffused (Edwin, 1987).

Atherosclerotic plaques vary in composition. Their major components include smooth muscle cells, cholesteryl esters and other lipids, collagen and glycosaminoglycans. In patients dying of myocardial infarction and in most instances of sudden cardiac arrest the great majority have severe extensive coronary atherosclerosis. Superadded coronary thrombosis is usually present in the vessel supplying the site of full thickness myocardial infarction; and increasing evidence indicates a role of localised coronary spasm in precipitating at least some acute occlusions (Lewis, 1988).

RELATION BETWEEN HYPERLIPIDEMIA AND ISCHAEMIC HEART DISEASE

The association between hyperlipidemia and ischaemic heart disease is beyond dispute. The probability that this association is one of cause and effect is suggested by various sources of evidence(Kannel et al,1971; 1979; Westlund et al, 1972; Martin et al, 1986; Hiroyasu et al, 1989; Edwin, 1990 and Lewis, 1988).

Coronary lesions closely resembling human atherosclerosis are inducible in primates and other animals in which hyperlipidemia is induced by high fat, high cholesterol diets. Such lesions show considerable regression when cholesterol levels are reduced by dietary change or medication (Kannel et al, 1979).

A comparison of several trials by Peto (1981) suggests that the extent of reduction in risk is directly related to the degree of reduction in plasma cholesterol.

Clinical trials in selected patients seem to indicate that effective modification of risk factors (e.g. High cholesterol) can slow the growth of coronary atherosclerosis (Edwin, 1990).

Serum cholesterol levels are positively correlated with diastolic blood pressure, which again is a risk factor for ischaemic heart disease(Hiroyasu et al, 1989).

Hypercholesterolemia indicative of high levels of LDL, has been identified as a major independent risk factor for ischaemic heart disease. Hypertriglyceridemia with raised VLDL is also associated with a higher incidence of coronary heart disease, but itself is less definite a predictor of atherosclerotic heart disease (Tripathi et al, 1990).

Risk of development of ischaemic heart disease has been shown to be a graded function of levels of total plasma cholesterol and more particularly so of LDL cholesterol (Tripathi et al, 1990).

On the other hand recent studies reveal a strong and independent inverse correlation between levels of HDL and HDL cholesterol with incidence of coronary heart disease. Higher the proportion of HDL cholesterol to total cholesterol lesser is the risk of vascular disease (Kannel et al, 1979).

The association of total cholesterol with IHD mortality and morbidity appear to derive chiefly from the LDL fraction with which it is highly correlated. Low levels of total or LDL cholesterol appear to be associated with an increased risk of non-cardiovascular deaths (Chiefly cancer). But studies in two populations - London and Paris - indicate that this inverse portion is confined to deaths in the very early years of the follow-up (Mann et al, 1987).

Increase in total triglycerides and levels of VLDL are usually associated in prospective studies with an increased IHD rate. This increased risk is apparent when triglyceride levels are higher than 150 mg/dl, but only two studies (both Scandinavian) have suggested that the association is independent of other measures of lipid metabolism (Mann et al, 1987).

Recent interest has centred around the possibility that HDL may be a protective factor. Where HDL has been measured in prospective studies, low levels do seem to be productive of subsequent IHD, and in communities where IHD is uncommon HDL levels are high. In people over 50 years

of age the predictive value of HDL appears to be stronger than that of LDL. Below the age of 50 it seems that the LDL might be more important predictor (Mann et al, 1987).

TREATMENT OF HYPERLIPIDEMIA

Abundant evidence has accumulated to show that treatment of hyperlipidemia will diminish or prevent atherosclerotic complications including ischaemic heart disease (Kannel et al, 1979; Lewis, 1988; Edwin, 1990, Lipid Research Clinics Programm, 1984a, 1984b). Numerous population studies have shown that an elevated concentration of total cholesterol or LDL cholesterol in plasma constitutes a major risk factor for the occurrence of atherosclerotic events (Goldstein et al, 1973; Keys, 1975; Hiroyasu et al, 1989 and Martin et al, 1986).

In 1984, the result of the Lipid Research Clinics Coronary Primary Prevention trial, a multicentre, randomized double blind study, provided strong evidence that a reduction in plasma concentrations of LDL cholesterol can reduce the risk of coronary artery disease (Lipid Research Clinics Program, 1984a, 1984b).

These conclusions were confirmed in 1987 by Helsinki Heart Study which showed that treatment of men with more moderate hypercholesterolemia (mean total cholesterol 289 mg/dl) could reduce the incidence of coronary events.

The drug used was gemfibrozil, and the clinical benefits were correlated with a fall in LDL cholesterol,

an increase in HDL cholesterol, and a decrease in plasma triglycerides.

Analysis of the relationship between cholesterol and coronary artery disease suggests that a 25% reduction of the total cholesterol in plasma would reduce the incidence of coronary events by nearly 50% (Lipid Research Clinics, Program, 1984b).

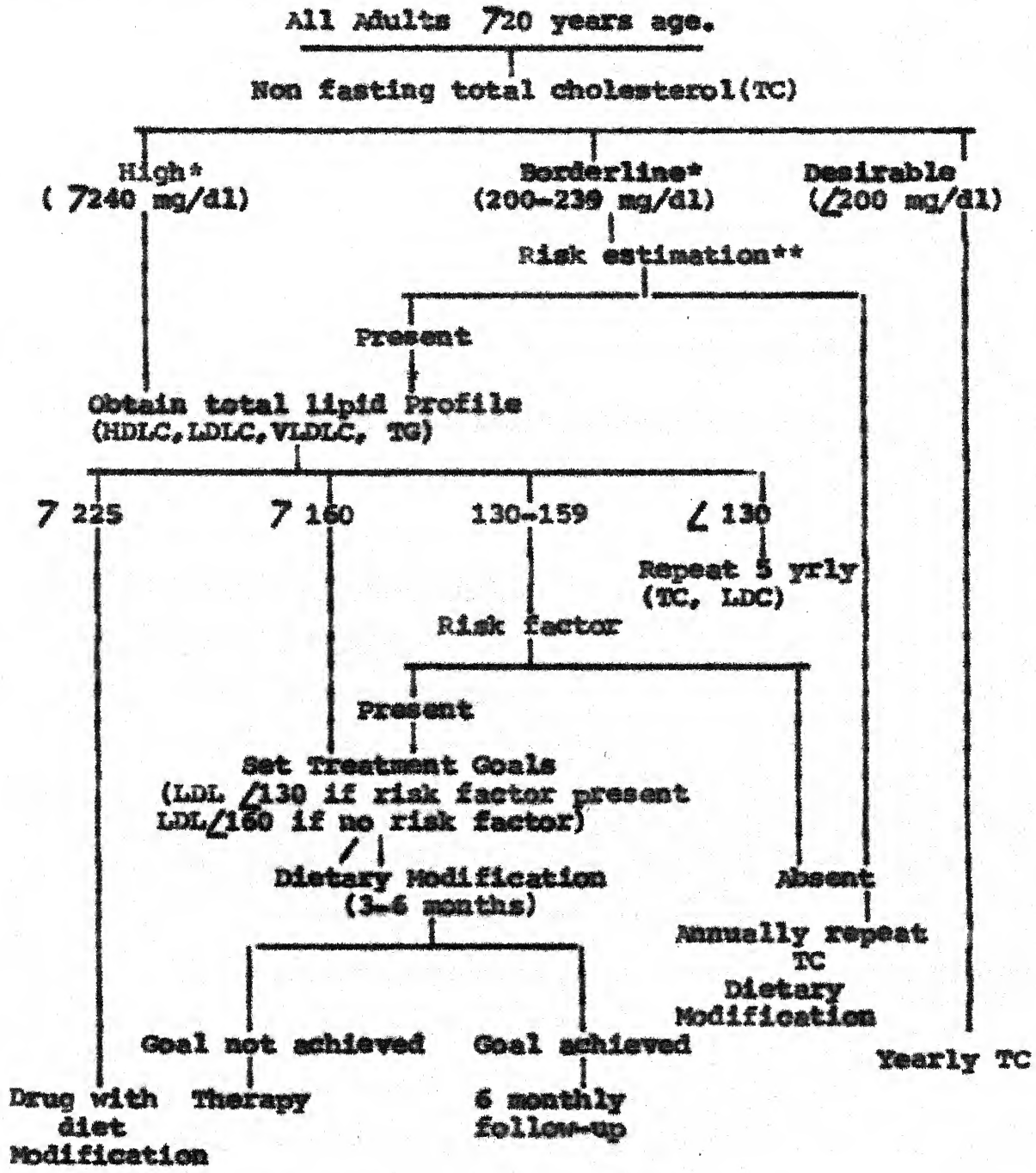
Epidemiological studies have revealed a negative correlation between the plasma concentration of HDL, which normally accounts for 20-30% of the total plasma cholesterol and the risk of coronary artery disease (Miller, 1980). In hypertriglyceridemic individuals frequently having low concentration of HDL, when treated with drugs that lower VLDL concentrations, the HDL will often return to normal levels. The fibric acids and HMG CoA reductase inhibitors raise HDL and lower LDL.

Recently few herbal drugs have been reported to have potent hypolipidemic effect. These include Commiphora mukul Hook ex Stocks, Terminalia arjuna W & A, Inula racemosa Hook. Panchacole (group of five herbs), etc (Sharma et al, 1990, Agarwal et al, 1986; Tiwari et al, 1990; Satyavati, 1987; Dwivedi et al, 1988).

Terminalia arjuna W & A has been reported to decrease LDL but at the same time it increases HDL cholesterol concentration in rabbits (Pathak et al, 1990; Dwivedi et al, 1988).

AIMS OF TREATMENT

Ultimate aim is to reduce the risk of CAD as low as possible. On the basis of present knowledge, NCEP recommends a TC level of 200 mg/dl and LDL level 130 mg/dl as desirable. A simplified approach on the basis of NCEP recommendation is as follows :



* Repeated measurements.

** Risk factors - Definite CAD (by history or investigations)

- Others
  - Male sex.
  - Family history of CAD(MI or sudden death of its parents of siblings before 55 years of age)
  - Cigarette smoking
  - Hypertension
  - Low HDL cholesterol (⁄35 mg%)
  - Diabetes mellitus
  - History of atherothrombotic stroke or peripheral vascular occlusive disease.
  - Obesity ⁄30% over weight

Risk factor 'present' indicates either definite CAD or 2 other risk factors.

PRESENT MANAGEMENT STRATEGIES

1. Lifestyle Measures

   i) Reduction of obesity.

   ii) General lipid lowering diet

   a. Saturated fatty acids ↓

   b. Cholesterol ↓

   c. Polyunsaturated fatty acids ↑

   d. Complex Carbohydrate ↑

   e. Soluble dietary fibre ↑

   iii) Chylomicronaemia diet

   a. All long chain fatty acids ↓

   b. Medium chain triglyceride ↑ I

   iv) Regular appropriate aerobic exercise.

2. Drugs

i) Cholesterol lowering

a. Cholestyramine
b. Cholestipol
c. Probucol
d. Mevinolin

ii) Triglyceride and cholesterol lowering

a. Nicotinic acid and derivatives.
b. Benzafibrate
c. Gemfibrozil

3. Invesive procedures

i) Partial ileal bypass.
ii) LDL-aphoresis.
iii) Plasma exchange.
iv) Portacaval shunt.

THE PRESENT DRUG COMBINATION

Each capsule contains :

Terminalia arjuna W & A bark (extract of)	500 mg
Inula racemosa Hook Root (extract of)	500 mg
Commiphora mukul Hook ex stock resin	500 mg

MODES OF ACTION

Though exact mode of action of T. arjuna, I. racemosa and gum resin of C. mukul are not known, yet on the basis of above mentioned facts and the researches conducted

so far on these plants, few hypotheses regarding the mode of action of each of them, may be offered.

Terminalia arjuna

It increases the levels of HDL cholesterol, which has protective role against atherogenesis (Tiwari et al, 1990).

PGE_2 is known to induce coronary vasodilation and hypotension. It also inhibits platelet aggregation. T arjuna enhances PGE_2 like activity thus it might help in preventing myocardial ischaemia (Dwivedi et al, 1987;1988).

It causes significant decrease in circulating catecholamine levels, while in adrenal glands its concentration goes up, thus, it might be acting by inhibiting the catecholamine release from adrenal glands into circulation, thus protecting the heart from catecholamine toxicity (Pathak et al, 1987).

It Possesses antihypertensive and antiarrhythmic activity, delays myocardial ischaemia in pre-treated animals (Dwivedi et al, 1988).

It Negative inotropic and negative chronotropic action on isolated spontaneously beating rat atrium (Srivastava et al, 1989).

It Increases cardiac output and accentuates auricular and ventricular contraction (Gupta et al, 1976).

It Reduces total cholesterol and triglycerides in blood and increases HDL cholesterol (Tiwari et al, 1990; Pathak et al, 1990).

Anti thrombotic, antiarrhythmic and antihypertensive action (Pathak et al, 1987).

All these activities, particularly hypolipidemic, enhancement of PGE_2 like activity, negative inotropic and chronotropic, antiarrhythmic, antihypertensive and HDL cholesterol raising properties contribute to its cardioprotective action.

Inula racemosa Hook

- Significant enhancement of PGE_2 like activity and thus preventing platelet aggregation (Dwivedi et al, 1987).
- Negative inotropic and negative chronotropic activity on normal as well as atropinized frog's heart (Sharma et al, 1986).
- Potent hypolipidemic and cardioprotective activity (Dwivedi et al, 1988).
- Lowering of diastolic blood pressure, anginal episodes, lowering catecholamine and cortisol levels (Dwivedi et al, 1989).
- Antianginal property (Tripathi et al, 1984a).

Thus hypolipidemic, hypoglycaemic, hypotensive, lipid lowering and catecholamine and cortisol lowering properties, besides significant enhancement of PGE_2 like activity thus preventing platelet aggregation may constitute its mode of action.

Gum resin of C. mukul Hook ex Stocks

- Fraction A of gum guggulu reduced the serum cholesterol levels and the pool size by :
  (i) a significant increase in the rate of removal/ extraction of cholesterol from the body.
  (ii) causing mobilization of cholesterol from the tissues (as evident clinically by the resolution of xanthomas).
  (iii) decrease in input/synthesis of cholesterol (Malhotra et al, 1973; 1974).
- Increasesx the rate of degradation of cholesterol by activating the thyroid gland (Tripathi et al, 1975).
- Since crude drug contains ion exchange resins, it is capable of combining with the bile acids and thereby trapping it out of intrahepatic circulation (Satyavati, 1966).

All of the above factors constitute the mode of action of gum resin of C. mukul regarding its potent hypolipidemic action.

CLINICAL STUDIES

1. C. mukul

Guggulu (Gum resin of C. mukul) has been used in medicine since times immemorial. It has been highly praised for its medicinal value in Atharvaveda, which is supposed to be the source of Ayurveda (Atharvaveda Kand 19 Sutra 38). Charak has enlisted it with the class of drugs useful for

regaining consciousness (Sangyasthapan) while Sushruta and Vagbhatta have included it in Eladigana (Sushruta Sutra 38/24). Charaka, Sushruta and Vagbhatta all the three reputed physicians of the past have mentioned that if a person develops complications because of excessive use of sneha (Snehavyapada and medoroga), he sould be treated with guggulu.

Taking lead from an obscure Sanskrit Shloka in Sushruta Samhita (Sutrasthanam : 15:32) Satyavati (1966) was the first to study guggulu on various experimental and clinical parameters at Banaras Hindu University. A thorough study by other workers followed for about 20 years and finally the drug was released in 1987 by Prime Minister of India at CDRI, Lucknow.

Preliminary clinical studies were carried out on 22 patients of hypercholesterolemia with associated obesity ischaemic heart disease, hypertension, diabetes etc. Crude guggulu was administered orally in a dose of 6-12 g. in 3 divided doses for 15 days to 1 month. A fall in total serum cholesterol and serum lipid phosphorus was noted in all the cases treated with guggulu. The body weight also revealed a significant decline in 10 patients of obesity (Satyavati, 1966; Dwarkanath and Satyavati, 1970).

Further, studies in 12 cases of hyperlipidemia (9 associated with obesity, 2 ischaemic heart disease and 1 case of cerebral thrombosis) showed that oral administration of 12 g of crude guggulu in 3 divided doses for

one month effectively lowered the serum turbidity and prolonged coagulation time in all the patients (Tripathi et al, 1968).

Clinical efficacy of fraction A of gum guggulu as hypolipidemic agent was evaluated in comparison to ethyl-p-chlorophenoxy isobutyrate and CIBA-13437-Su. Forty-four patients classified according to Frederickson's classification were administered these drugs, the selection of patients for each drug being made at random. Fraction A of gum guggulu was administered in the dose of 1.0 g in two divided doses daily. The duration of treatment varied from 6 to 34 weeks. Statistical analysis revealed that fraction A lowered significantly the serum levels of all the lipid fractions (serum total lipids, triglycerides, cholesterol, phospholipids and beta lipoprotein). The lowering of triglycerides was found most encouraging in case of gum guggulu in comparison to all the known drugs. The side effects observed were hiccough in one patient, diarrhoea in three patients and restlessness and apprehension in one patient (Malhotra et al, 1971).

Faecal sterol studies in 12 cases of hyperlipoproteinemia indicated that both fraction A of guggulu as well as clofibrate enhanced the faecal excretion of sterols by 59% and 49.3% respectively. This long term study indicated that the hypolipidemic effect of fraction A of guggulu could be attributed to : (a) increase in the rate of removal/ excretion of cholesterol via gut (b) decrease in the input/

synthesis of cholesterol and (c) mobilization of cholesterol from tissues (Malhotra, 1973).

To elucidate the effect of fraction A on cholesterol metabolism, kinetic studies with 4-C^{14} cholesterol were carried out separately in two series. In the first the effect of drug was investigated without attaining isotopic equilibrium, whereas in the second, the studies were conducted after attaining isotopic steady state (i.e. after studies). From the data of this experimental study in rats it could be interpreted that fraction A enhanced the rate of excretion of cholesterol considerably and also reduced the input/synthesis of cholesterol. The cholesterol pool size also decreases after administration of fraction A. Similarly clofibrate inhibited the rate of input/synthesis of cholesterol and increased its rate of excretion significantly. In human studies also fraction A of guggulu reduced the serum cholesterol levels and the pool size by causing (i) significant increase in the rate of excretion of cholesterol and (ii) mobilization of cholesterol from tissues (as evident by resolution of xanthomas clinically (Malhotra et al, 1974).

The effect of guggulu on body weight was studied by Sidhu and associates (1976). In the study 60 obese patients with hyperlipidemia were administered guggulu in the dose of 4 g/day for 8 weeks. Significant reduction of 2.34 kg in body weight was observed in first 4 weeks after that the weight reduction became insignificant. Skin folds

of triceps, subscapsular and calf have shown reduction of general and biceps in particularly.

Guggulu was tried on 25 patients of coronary insufficiency. 12-16 g/day of drug was administered for 12 weeks. Serum cholesterol was found to be reduced by 27.8% and triglycerides by 32.7%. Depression of ST segment and correction in T. wave inversion was observed in ECG of all the patients of coronary insufficiency (Upadhyaya et al, 1976).

The effect of the drug was studied on 75 patients of obesity associated with other lipid disorders besides arthritis and diabetes mellitus. The dose given was 6-8 g of guggulu per day for a duration of 12 weeks. Fall in body weight was observed at the rate of 1 kg per month. Reduction in total serum cholesterol was found to be 24.5% and serum turbidity was reduced by 15.88%. At the same time coagulation time of blood was noticeably increased by 68.8%. This last finding is important in consideration of administration of the drug in the patients of atherosclerotic heart disease (Tripathi et al, 1976).

In a long term clinical study, 41 cases of hyperlipoproteinemia were followed up after therapy for 75 weeks with fraction A of guggulu 1.5 g/day. Ten cases were treated with clofibrate 2.0 g/day for a mean period of 75 weeks. Statistically significant reduction was observed in total cholesterol (36.8%) and triglycerides (50.4%) with

fraction A while clofibrate also reduced total cholesterol (43.5%) and triglycerides (50.2%). Guggulu resolved completely xanthomas in three cases while clofibrate resolved in one out of three cases. Neither fraction A nor clofibrate was found to reduce the body weight. Except milk diarrhoea in 5 cases no other side effects were observed with guggulu (Malhotra et al, 1977).

Fraction A of guggulu in the dose of 1.0 g/day was found to reduce the total blood cholesterol by 4.5% (Kuppurajan et al, 1978).

Guggulu given in the dose of 12-16 g/day for 12 weeks to 25 patients of hyperlipidemia with associated disorders was reported to reduce the cholesterol by 35.8% in 96% cases, triglycerides by 32.76% in 88% cases, free fatty acids by 62.12% and serum phospholipids by 40%, besides reducing the body weight at the rate of 1.4 kg per month (Gupta et al, 1978).

Guggulipid in the dose of 1.2 g/day for 6 weeks reduced cholesterol by 15% and triglycerides by 20% (Saxena, 1980), while in another study where guggulipid was administered in the dose of 1.5 g/day for 12 weeks it was redorded to bring down the levels of cholesterol by 16.9% and triglycerides by 27.13% (Agarwal et al, 1986).

Upadhyaya and coworkers (1982) studied the effect of guggulu powder on a long series of patients. Guggulu powder in the dose of 8 g/day was administered to 135 patients of ischaemic heart disease for a duration of 12

weeks. Complete improvement in precordial pain was noted in 75% of patients, and in dyspnoea on effort in 72% of cases. Reduction in body weight was found to be 1 kg per month. 14% of patients showed complete improvement in ECG changes of ischaemic heart disease. Biochemical investigation in these patients revealed reduction in serum cholesterol (27%), serum triglycerides (36%), phospholipids (20%) and free fatty acids (37%). Its hypolipidemic effect was found to be better than that of clofibrate.

Fraction A of guggulu administered in the dose of 1.5 g/day for 12 weeks to 85 patients of hyperlipidemia and allied disorders showed significant reduction in body weight in first four weeks specially in relation to triceps folds. Significant reduction in total serum cholesterol, total lipids and triglycerides levels was also observed (Kotiyal, et al, 1984).

A 1:1 combination of Guggulu and Pushkara moola (I. racemosa) was assessed for its clinical efficacy on the patients of ischaemic heart disease. The drug was dispensed in the dose of 6 g/day for 16 weeks to 50 patients of ischaemic heart disease. The results showed that 10% cases were cured (no precordial pain, and serum lipids and ECG abnormalities normalised). 60% patients relieved (improvement only in precordial pain), however, no improvement was observed in the remaining 10% of cases. The combination lowered total serum cholesterol level by 17.47% (Tripathi et al, 1984).

Guggulipid in the dose of 1.2 g/day was given to 23 patients of hyperlipidemia with hypertension, IHD, diabetes mellitus, diabetes mellitus with hypertension, IHD with hypertension and gout, for a period of 4 weeks. The aim of the study was to evaluate the safety of the drug on long term administration of human beings. The drug was found to be completely safe and did not produce any alteration in hepatic or renal functions blood sugar levels, haematological parameters and electrocardiogram. It significantly lowered the serum cholesterol by 27.4% and triglycerides by 48.7% in 78.9% of patients (Agarwal et al, 1986).

Thus the significant reduction in serum cholesterol triglycerides, phospholipids and free fatty acids, improvement of ECG abnormalities, reduction of weight and no side effects besides the lipid lowering capacity being comparable to presently available drugs, justifies the inclusion of guggulu in the present formulation.

2. T. arjuna

Vagbhatta (700 A.D.) was the first to advocate the use of T. arjuna in cardiac ailments. He prescribed the use of bark powder. He did not mention any specific cardiac disorder in which it could be more effective. Later on Chakradatta(1700) advised it for "burning of the chest". He prescribed the powder of the outer coating of the bark diluted with milk for the "relief of pain caused by heart".

a condition similar to that of the present day angina pectoris. In addition he also prescribed its administration with water or ghee. Bhavamishra (1700) a contemporary of Chakradatta also advised the use of bark powder of T arjuna in chest pain due to cardiac ailments.

Its use in congestive heart failure was prompted mainly by cardiotonic property attributed it. However, it did not have any effect on it except for a mild diuretic action (Koman, 1920; Ghosh, 1926; Gaius et al, 1938). Colabewalla (1951) found the decoction of T arjuna bark to be more useful in hypertensive heart disease compared to congestive heart failure. This apparently made it clear that the drug might be acting through other mechanism apart from its diuretic action. The initial belief of its cardiotonic property obviously could not be validated in these studies. The attention was then diverted to its utility on ischaemic heart disease. Chaturvedi (1973) first used alcoholic decoction of bark in stable cases of ischaemic heartt disease and found that the prolonged use of this drug brings sense of well being and increases euglobulin lysis time and prothrombin time. He also described electrocardiographic improvement following the use of this drug. Subsequently another report about its utility in complete heart block of ischaemic etiology has been published. This particular patient, an adult male who developed stokes Adam's attacks following chest pain.

became well after 3 months use of crude powder of T. arjuna (Udupa, 1986). Recently in another study 500 mg crude drug powder of T. arjuna was administered in 30 patients of stable angina pectoris. The drug was useful in alleviating the anginal pain. It was also noted to be useful in the cases of ischaemic heart disease associated with rhythm disturbances, particularly premature beats. The drug was found to be beneficial in modifying various known coronary risk factors like obesity, hypertension, diabetes mellitus, and circulating catecholamines in these patients. No significant side effects were observed by these workers. This study has further corroborated the ancient observation of the usefulness of T. arjuna in cardiac pain. Ambasta (1986) found the drug to be effective in hypertension. Dwivedi (1988) confirmed the efficacy of the drug in reducing intensity and frequency of angina pectoris, improvement in effort tolerance, modification of myocardial ischaemia risk factors and cardioprotective action.

3. I. racemosa

Charak Samhita (Old Ayurvedic text book of medicine) was the first to advocate the administration of I. racemosa root podwer to the patients of hiccough, asthma and pain on sides of chest (parshwashoola, angina pectoris). Later Bhavamishra (author of Bhaveprakash Nighantu) also referred to its beneficial effects in anginal pain. Chopra et al (1956) has mentioned it to be used as expectorant and

resolvement of indurations. Uniyal (1982) wrote about its efficacy in 'Vatarogas'(disorders characterised by different types of pains and neurological diseases).

Water extract of I. racemosa roots was used in a series of 44 patients and showed improvement in pulmonary functions, haematological picture and general health (Singh et al, 1983).

Probably taking a lead from Charak and Bhavamishra the drug (root powder) was tried in 9 patients of ischaemic heart disease. It showed significant prevention of post exercise S-T segment depression in all the patients of ischaemic heart disease and results were found to be comparable to nitroglycerine (Tripathi et al, 1984a). Further, a combination of root powder of I racemosa and oleo gum rasin of C. mukul(Guggulu) in the dose of 6000 mg/day was given to 50 patients of ischaemic heart disease. It completely cured 5 patients, significant improvement in ECG patient was noted in 40 patients and 5 patients failed to respond to drug (Tripathi et al, 1984b).

In a study on a series of 60 patients the water extract of I. racemosa was given in the dose of 1500 mg/day. Significant reduction in number of episodes of angina pectoris, significant improvement in ST depression and T wave inversion in ECG of the patients were important observations, however, it had no significant effect on blood pressure (Dwivedi et al, 1989).

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was conducted on 30 subjects from three sources :

1. Those admitted in the medical wards of M.L.B. Medical College, Hospital, Jhansi.
2. Those attending the Out Patients' Department of M.L.B. Medical College, Hospital, Jhansi.
3. Those residing in the BHEL Township, Jhansi.

All subjects had their initial serum cholesterol above 200 mg/dl.

Out of 30 subjects, only 8 were females. The age range was from 28 to 65 years with an average of 45±10 years. Their weight was ranging from 52 to 86 kg with a mean of 66±6 kg. The height was from 145.0 to 170 cms, the mean±S.D. being 160.3±7.0 cms.

Detailed history revealed that 3 subjects were suffering from diabetes mellitus, 7 from coronary artery disease (CAD) and 2 from hypertension, while 5 were suffering from a combination of above. Rest of the 13 subjects were not having any of the above diseases.

Family history revealed a positive history of hypertension, diabetes and/or coronary artery disease in one or both the parents in 14 subjects. While some of the healthy subjects gave positive family history, there were others with disease but negative family history.

Personal and dietary histories were also varying to a great extent. Only 7 subjects were smokers and 5 were alcoholic. Out of 30 subjects, 13 did not use saturated fats in their diet whereas 20 persons used polyunsaturated fats. Two subjects did not use milk. Half of the subjects liked eggs. Only 8 persons liked meat.

DESIGN OF TEST

Informed consent was taken from all the subjects. The subjects were asked to have their normal dinner on the previous night and not to take anything after this except water. Next morning fasting blood sample was taken. Then the subjects were asked to take the drug in a regular dosage of two capsules twice daily for 3 months. Similar monthly blood samples were taken. During the study period they were told not to change their dietary or personal habits as this could otherwise have effect on the lipid profile.

Serum was separated from the blood samples and following tests were performed:-

A. SERUM TOTAL CHOLESTEROL (STC)

It was estimated by following method using chemical kits of Ethnor.

1. Added 5 ml of cholesterol reagent in each of three test tubes name T, S and B for 'test', Standard and Blank respectively.

2. To this added 25 ul of serum, cholesterol standard (250 mg/dl) and distilled water in T, S and B respectively.
3. Mixed them well for 10 seconds and placed in a boiling water bath for exactly 45 seconds.
4. Cooled them immediately in running tap water and mixed their contents.
5. Optical densities were read at 560 nm, setting the blank as zero.
6. Serum cholesterol calculated by the formula :

$$\text{STC (mg/dl)} = \frac{\text{Optical Density of Test}}{\text{Optical Density of Standard}} \times 250$$

B. SERUM TRIGLYCERIDES (STG)

It was estimated by using enzymatic kits of Ethnor employing following method :

1. Reconstituted each vial of reagent I (supplied in the form of lyophilised enzymes) in 2.5 ml distilled water.
2. Took 0.5 ml of reconstituted reagent I in each of three test tubes labelled T, S and B for test, Standard and Blank respectively.
3. To this added 0.5 ml of reagent II (Phenol solution) in each of three test tubes labelled T, S and B and mixed them all well.
4. To this added 20 ul of serum triglyceride standard(300 mg/dl) and distilled water in T, S and B respectively, mixed well and incubated at 37°C ±0.5°C for 10 minutes.

5. Finally 2 ml of distilled water was added to all three tubes, mixed and reading taken at 500 nm setting the blank at zero.
6. Triglyceride calculated by using the formula :

$$\text{STG (mg/dl)} = \frac{\text{Optical Density of Test}}{\text{Optical Density of Standard}} \times 300$$

C. ESTIMATION OF HDL CHOLESTEROL

It was also estimated by using the enzymatic kits of Ethnor by following method :

1. To precipitate the LDL and VLDL cholesterol and chylomicrons, mixed 0.5 ml of lipogent reagent with equal amount of serum and kept at room temperature($25\pm5^{o}C$) for 10 minutes. Then centrifuged it at 2000 rpm for 20 minutes.
2. Working standard was prepared by diluting the provided standard with distilled water in the ratio of 1 : 7.
3. Working reagent was prepared by mixing the reagent I lyophilised enzymes) with reagent II(Phenol solution).
4. Took 1.0 ml of working reagent in each of three test tubes labelled T, S and B for Test, Standard and Blank respectively.
5. To this, added 100 ul of supernatant (obtained in step 1), working standard and distilled water to T, S and B respectively and mixed them well.

6. After incubating all the tubes at 37°C for 15 minutes added distilled water 4.0 ml to each and reading taken at 515 nm after mixing the tubes well and setting the Blank at zero.

7. HDL cholesterol calculated by the formula :

$$\text{HDL (mg/dl)} = \frac{\text{Optical Density of Test}}{\text{Optical Density of Standard}} \times 50$$

D. LDL ESTIMATION

LDL cholesterol was directly calculated by Friedwald's formula:

$$\text{LDL (mg/dl)} = \text{STC} - (\text{STG}/5 + \text{HDL})$$

Simultaneously, routine biochemical tests were done at monthly intervals to check any associated change in these parameters.

O B S E R V A T I O N S

OBSERVATIONS

The present study was carried out on 30 subjects with hypercholesterolaemia. They were given the hypolipidemic drug in a regular dosage of two capsules twice a day for 3 months. Only 22 subjects could complete the trials. Rest of the 8 dropped at varying intervals on account of one or the other reasons. Basal and monthly blood samples were collected and lipid profile done. Before analysing the data, the subjects were grouped into 2 pairs.

1. On the basis of initial serum total cholesterol, they could be divided into those having initial STC below 250 mg/dl and those above it.
2. On the basis of presence or absence of coronary artery disease (CAD).

Now, these data were analysed for :

1. Any change in different parameters of lipid profile inducible by the drug in all subjects in different groups.
2. Comparison of this change in different groups.

Note : For the sake of effective comparison the data from the dropped cases were not analysed but have been mentioned here as it signifies the compliance with which the subjects have taken the drug.

SERUM TOTAL CHOLESTEROL(STC) : TABLE I

TABLE I : Serum cholesterol values of subjects receiving the drug C.T.I.

Sl. No.	Name	Serum total cholesterol(mg/dl) 0 month	1 month	2 months	3 months
1.	SAN	265	250	250	240
2.	H	267	260	255	250
3.	R	230	228	215	200
4.	RM	228	220	220	200
5.	BMT	292	283	270	250
6.	MPG	250	232	240	230
7.	SR	243	250	230	225
8.	I	245	196	205	214
9.	BM	430	201	238	222
10.	RSVP	230	225	245	240
11.	AKS	235	244	240	238
12.	SN	226	230	220	210
13.	GD	250	240	240	230
14.	KV	280	275	250	260
15.	SS	240	250	250	250
16.	AA	280	275	250	260
17.	VP	230	250	250	240
18.	RS	260	250	255	240
19.	NK	265	250	255	240
20.	SK	260	235	240	230
21.	ST	225	230	225	225
22.	SS	270	250	215	220
	Mean	259	241	236	230
	±S.D.	±43	±20	±17	±16

't' test : 0 : I month $p < 0.05$
0 : II months $p < 0.05$
0 : III months $p < 0.005$
I : II months $p > 0.05$
I : III months $p < 0.05$
II : III months $p > 0.05$

The basal STC of the subjects ranged from 226 mg/dl to as high as 430 mg/dl. But all except one values were from 226 to 292 mg/dl. The mean ±S.S. came to 259±43 mg/dl. After 1 month of therapy this value came down to 241±20 mg/dl and the change was statistically significant (p $<$0.05). After another 1 month it further reduced to 236±17 mg/dl, but the change between 1-2 months was insignificant (p $>$0.05).

After 3 months of completion, the final STC value was 230±16 mg/dl and this had significantly changed from 1 month value as well (p $<$0.05). If we compare the 3 months' value with the basal STC, we see that the change is highly significant(p $<$0.005). The total fall was 11.2%.

STC CHANGES IN DIFFERENT GROUPS

1. In subjects with coronary artery disease as one of the complications of hypercholesterolaemia, the mean ± S.D. of basal STC values was 268±67 mg/dl and it apparently fell to 236±18 mg/dl after one month and then to 237±12 mg/dl after two months. The final value was 227±14 mg/dl. But as the group is too small, this fall comes to be statistically insignificant (p $>$0.05), though seemingly drastic i.e. 15.3% (Table II).

TABLE II : Serum total cholesterol values of subjects having CAD as one of the complications of hypercholesterolaemia.

Sl. No.	Name	Serum total cholesterol (mg/dl) 0 month	1 month	2 months	3 months
1.	RM	228	220	220	200
2.	SR	243	250	230	225
3.	BM	430	201	238	222
4.	GD	250	240	240	230
5.	SS	240	250	250	250
6.	RS	260	250	255	240
7.	NK	265	250	240	225
8.	ST	225	230	225	225
	Mean ±S.D.	268 ±67	236 ±18	237 ±12	227 ±14

't' test : 0 : I month $p > 0.05$
0 : II months $p > 0.05$
0 : III months $p > 0.05$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

2. The basal cholesterol in subjects not having coronary artery disease was 254±22 mg/dl and it fell to 243±22 mg/dl, though statistically insignificant ($p > 0.05$), after 1 month, and again to 236±20 mg/dl after 2 months of treatment. The difference was significant ($p < 0.05$) as compared to the basal value. The final value was 231±17 mg/dl and it is significantly different from basal value ($p < 0.01$). The total fall was 9% (Table III).

TABLE III : Serum total cholesterol values of subjects not having CAD.

Sl. No.	Name	Serum total cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	265	250	250	240
2.	H	267	260	255	250
3.	R	230	228	215	200
4.	BMT	292	283	270	250
5.	MPG	250	232	240	230
6.	I	245	196	205	214
7.	RSVP	230	225	245	240
8.	AKS	235	244	240	238
9.	SN	226	230	220	210
10.	KV	280	250	210	215
11.	AA	280	275	250	260
12.	VP	230	250	250	240
13.	SK	260	235	240	230
14.	SS	270	250	215	220
	Mean ±S.D.	254 ±22	243 ±22	236 ±20	231 ±17

't' test : 0 : I month $p > 0.05$
0 : II months $p < 0.05$
0 : III months $p < 0.01$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

3. Table IV shows that there was no significant change in serum total cholesterol levels in those persons who had basal values below 250 mg/dl even after full 3 months of drug treatment ($p > 0.05$).

TABLE IV : Serum total cholesterol changes in subjects with initial levels below 250 mg/dl.

Sl. No.	Name	Serum total cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	R	230	228	215	200
2.	RM	228	220	220	200
3.	SR	243	250	230	225
4.	I	245	196	205	214
5.	RSVP	230	225	245	240
6.	AKS	235	244	240	238
7.	SN	226	230	220	210
8.	SS	240	250	250	250
9.	VP	230	250	250	240
10.	ST	225	230	225	225
11.	Mean	233	232	230	224
	±S.D.	± 7	±17	±16	±18

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months

$p > 0.05$

4. In those subjects who had initial STC 250 mg/dl or above, it fell significantly from 281±49 to 248±21 mg/dl only after one month of drug therapy($p < 0.05$). It came to 242±17 mg/dl after 2 months and there was a significant fall between 1 to 3 months as well ($p < 0.05$) bringing the final value to 234±14 mg/dl. The change from basal to final values was highly significant($p < 0.001$)(Table V).

TABLE V : Serum total cholesterol changes in subjects with initial levels 250 mg/dl or above.

Sl. No.	Name	Serum total cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	265	250	250	240
2.	H	267	260	255	250
3.	BMT	292	263	270	250
4.	MPG	250	232	240	230
5.	BM	430	201	238	222
6.	GD	250	240	240	230
7.	KV	280	250	210	215
8.	AA	280	275	250	260
9.	RS	260	250	255	240
10.	NK	265	250	240	225
11.	SK	260	235	240	230
12.	SS	270	250	215	220
	Mean ±S.D.	281 ±49	248 ±21	242 ±17	234 ±14

't' test : 0 : I month $p < 0.05$
0 : II months $p < 0.05$
0 : III months $p < 0.01$
I : II months $p > 0.05$
I : III months $p < 0.05$
II : III months $p > 0.05$

INTERGROUP COMPARISON

1. Comparison between table II and III reveals that there was never a significant difference between the subjects who had CAD and those without it ($p > 0.05$).

't' test : at 0, I, II, and III months $p > 0.05$.

2. Comparison between table IV and V shows that there was significant difference initially ($p < 0.01$) as well as at one month ($p < 0.05$) but the difference was no more after 2 and 3 months ($p > 0.05$).

't' test : 0 month $p < 0.01$
I months $p < 0.05$
II months $p > 0.05$
III months $p > 0.05$

SERUM TRIGLYCERIDE (STG) : TABLE VI

The initial STG ranged from as low as 100 mg/dl to as high as 480 mg/dl with a mean $\pm$ S.D. of 206 ± 84 mg/dl. It came down to 199 ± 55 mg/dl at 1 month but the change was not significant ($p > 0.05$). At 2 months it rose again to 210 ± 59 mg/dl but still the change was not significant ($p > 0.05$) and the final value was 196 ± 58 mg/dl which did not differ from STG value at any stage of the drug trials ($p > 0.05$).

TABLE VI : Serum triglyceride values of subjects receiving the drug C.T.I.

Sl. No.	Name	Serum Triglyceride (mg/dl) 0 month	1 month	2 months	3 months
1.	SAN	480	300	350	300
2.	H	110	115	150	100
3.	R	200	200	250	200
4.	RM	172	150	160	150
5.	BMT	195	190	225	200
6.	SR	180	200	200	200
7.	MPG	300	240	250	225
8.	I	190	154	150	162
9.	BM	340	300	250	260
10.	RSVP	180	225	292	250
11.	AKS	203	200	196	218
12.	SN	160	180	150	150
13.	GD	120	100	130	125
14.	KV	200	200	200	180
15.	SS	140	180	180	200
16.	AA	200	180	200	160
17.	RS	140	160	160	160
18.	VRS	200	240	240	235
19.	NK	250	200	180	150
20.	SK	230	220	225	200
21.	ST	100	140	150	145
22.	SS	250	300	320	350
	Mean ±S.D.	206 ±84	199 ±55	210 ±59	196 ±58

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months

$p > 0.05$

STG CHANGES IN DIFFERENT GROUPS

1. The mean basal STG of subjects having CAD as one of the complications of hypercholesterolaemia was 180±79 mg/dl and it constantly fell to 179±59 mg/dl 176±37 and 174±44 mg/dl after 1, 2 and 3 months respectively. Values did not differ significantly from at one another/any stage (p 70.05).(Table VII).

TABLE VII : Serum triglyceride values in subjects having CAD as one of the complications of hypercholesterolaemia.

Sl. No.	Name	Serum Triglyceride (mg/dl) 0 month	1 month	2 months	3 months
1.	RM	172	150	160	150
2.	SR	180	200	200	200
3.	BM	340	300	250	260
4.	GD	120	100	130	125
5.	SS	140	180	180	200
6.	RS	140	160	160	160
7.	NK	250	200	180	150
8.	ST	100	140	150	145
	Mean ±S.D.	180 ±79	179 ±59	176 ±37	174 ±44

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months

p 70.05

2. Similarly the basal STG values of subjects not having coronary artery disease was 221±86 mg/dl and it reached to 210±50, 228±62 and 209±63 mg/dl at 1, 2 and 3 months respectively. Again no two values were statistically significant in their difference (p >0.05 at all stages)(Table VIII).

TABLE VIII : Serum triglyceride values of subjects not having CAD.

Sl. No.	Name	Serum triglyceride (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	480	300	350	300
2.	H	110	115	150	100
3.	R	200	200	250	200
4.	BMT	195	190	225	200
5.	MPG	300	240	250	225
6.	I	190	154	150	162
7.	RSVP	180	225	292	250
8.	AKS	203	200	196	218
9.	SN	160	180	150	150
10.	KV	200	200	200	180
11.	AA	200	180	200	160
12.	VP	200	240	240	235
13.	SK	230	220	225	200
14.	SS	250	300	320	350
	Mean ±S.D.	221 ±86	210 ±50	228 ±62	209 ±63

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
I : III months

p >0.05

3. The basal STG of those subjects with initial STC ⩽250 mg/dl ranged from 100 to 203 mg/dl with a mean± S.D. of 172±32 mg/dl. This value increased to 187±32 at 1 month and 197±49 mg/dl at 2 months and then slightly fell to 191±38 mg/dl after 3 months of treatment. However, there was no significant change at any stage(p ⩾0.05) (Table IX).

TABLE IX : Serum triglyceride changes in subjects with initial serum cholesterol levels between 200 to 249 mg/dl.

Sl. No.	Name	Serum triglyceride (mg/dl)			
		0 month	1 month	2 months	3 months
1.	R	200	200	250	200
2.	RM	172	150	160	150
3.	SR	180	200	200	200
4.	RSVP	180	225	292	250
5.	I	190	154	150	162
6.	AKS	203	200	196	218
7.	SN	160	180	150	150
8.	SS	140	180	180	200
9.	VP	200	240	240	235
10.	ST	100	140	150	145
	Mean ±S.D.	172 ±32	187 ±32	197 ±49	191 ±38

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months
p ⩾0.05

4. The basal STG of those subjects having STC 250 mg/dl or above ranged from 110 to 480 mg/dl with a mean of 235±103 mg/dl. It fell to 209±68 mg/dl after 1 month of treatment but the change was insignificant (p >0.05). It again rose to 220±66 mg/dl the change being statistically insignificant(p >0.05) and finally fell to 201±73 mg/dl but not significantly in terms of statistics(p >0.05)(Table X).

TABLE X : Serum triglyceride changes in subjects with initial serum cholesterol levels 250 mg/dl or more.

Sl. No.	Name	Serum triglyceride (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	480	300	350	300
2.	H	110	115	150	100
3.	BMT	195	190	225	200
4.	MPG	300	240	250	225
5.	BM	340	300	250	260
6.	GD	120	100	130	125
7.	KV	200	200	200	180
8.	AA	200	180	200	160
9.	RS	140	160	160	160
10.	MK	250	200	180	150
11.	SK	230	220	225	200
12.	SS	250	300	320	350
	Mean ±S.D.	235 ±103	209 ±68	220 ±66	201 ±73

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months

p >0.05

INTERGROUP COMPARISON

1. Comparison between table VII and VIII reveals no difference at any stage.

't' test : at 0, I, II, and III months p $>$ 0.05.

2. Similarly, comparison between tables IX and X reveals no difference at any stage (p $>$ 0.05).

't' test : 0 month p $>$ 0.05
I months p $>$ 0.05
II months p $>$ 0.05
III months p $>$ 0.05

HDL CHOLESTEROL : (TABLE XI)

The basal values ranged from 32 to 50 mg/dl with a mean of 40±5 mg/dl and it rose to 42±4 mg/dl after 1 month, but only insignificantly (p $>$ 0.05). After another one month no change was noticed as it remained at 42±4 mg/dl. But final value was 44±4 mg/dl which had increased significantly from the basal value (p $<$ 0.005). The total rise was 10% (Table XI).

TABLE XI : Serum HDL cholesterol values of subjects receiving the drug C.T.I.

Sl. No.	Name	Serum HDL Cholesterol(mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	40	45	45	45
2.	H	42	40	45	45
3.	R	35	35	40	42
4.	RM	32	35	38	35
5.	BMT	36	40	40	45
6.	SR	40	40	40	43
7.	MPG	40	43	40	45
8.	I	50	39	40	43
9.	BM	32	40	46	45
10.	RSVP	45	50	43	40
11.	AKS	40	41	40	44
12.	SN	35	37	40	40
13.	GD	50	50	50	50
14.	KV	40	43	43	45
15.	SS	35	38	35	40
16.	AA	38	38	40	43
17.	VP	40	40	40	40
18.	RS	45	43	45	48
19.	NK	45	50	48	50
20.	SK	40	43	45	45
21.	ST	40	43	40	40
22.	SS	38	40	45	50
	Mean	40	42	42	44
	±S.D.	±5	±4	±4	±4

't' test : 0 : I month p $>$ 0.05
0 : II months p $>$ 0.05
0 : III months p $<$ 0.005
I : II months p $>$ 0.05
I : III months p $>$ 0.05
II : III months p $>$ 0.05

HDL CHANGES IN VARIOUS GROUPS

1. The basal HDL of subjects having CAD as one of the complications of hypercholesterolemia was 40±7 mg/dl and it increased to 42±5, 43±5 and 44±5 mg/dl after 1, 2 and 3 months of therapy respectively, but as the group is very small the change could not be shown as statistically significant at any stage (p 70.05) (Table XII).

TABLE XII : HDL Cholesterol values of subjects having CAD as one of the complications of hypercholesterolemia.

Sl. No.	Name	Serum HDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	RM	32	35	38	35
2.	SR	40	40	40	43
3.	BM	32	40	46	45
4.	GD	50	50	50	50
5.	SS	35	38	35	40
6.	RS	45	43	45	48
7.	NK	45	50	48	50
8.	ST	40	43	40	40
	Mean ±S.D.	40 ±7	42 ±5	43 ±5	44 ±5

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months

p 70.05

2. Similarly, the basal HDL of those subjects having coronary artery disease was 40±4 mg/dl and it gradually increased to 41±4, 42±2 and 44±3 mg/dl after 1, 2 and 3 months of drug treatment respectively. The change was significant only after 3 months because of cummulative effect ($p < 0.01$) (Table XIII).

TABLE XIII : Serum HDL cholesterol values of subjects not having CAD.

Sl. No.	Name	Serum HDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	40	45	45	45
2.	H	42	40	45	45
3.	R	35	35	40	42
4.	BMT	36	40	40	45
5.	MPG	40	43	40	45
6.	I	50	39	40	43
7.	RSVP	45	50	43	40
8.	AKS	40	41	40	44
9.	SN	35	37	40	40
10.	KV	40	43	43	45
11.	AA	38	38	40	43
12.	VP	40	40	40	40
13.	SK	40	43	45	45
14.	SS	38	40	45	50
	Mean ±S.D.	40 ±4	41 ±4	42 ±2	44 ±3

't' test : 0 : I month $p > 0.05$
0 : II months $p > 0.05$
0 : III months $p < 0.05$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

3. The basal HDL of those subjects with initial STC below 250 mg/dl was 39±5 mg/dl. It slightly increased to 40±4 mg/dl at 1 month and remained at 40±2 mg/dl after 2 months after which it finally increased to 41±2 mg/dl. However, there was no significant change statistically at any stage ($p > 0.05$) (Table XIV).

TABLE XIV : HDL cholesterol changes in subjects with initial serum cholesterol between 200 to 249 mg/dl.

Sl. No.	Name	Serum HDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	R	35	35	40	42
2.	RM	32	35	38	35
3.	SR	40	40	40	43
4.	I	50	39	40	43
5.	RSVP	45	50	43	40
6.	AKS	40	41	40	44
7.	SN	35	37	40	40
8.	SS	35	38	35	40
9.	VP	40	40	40	40
10.	ST	40	43	40	40
	Mean ±S.D.	39 ±5	40 ±4	40 ±2	41 ±2

't' test : 0 : I month
0 : II months
0 : III months
I : II months
I : III months
II : III months

$p > 0.05$

4. The basal HDL of those subjects with initial serum total cholesterol levels 250 mg/dl or above was 40±5 mg/dl. After 1 month of drug therapy it increased to 43±4 mg/dl, but the change was not statistically significant ($p > 0.05$). After another month of continued treatment it went up to 44±3 mg/dl and now it was significantly higher than the basal value ($p < 0.05$). Finally it settled at 46±2 mg/dl which was markedly different from the basal value ($p < 0.005$). Also, there was a significant change between 1 to 3 months ($p < 0.05$) (Table XV).

TABLE XV : Serum HDL cholesterol changes in subjects with initial serum cholesterol 250 mg/dl or above.

Sl. No.	Name	Serum HDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	40	45	45	45
2.	H	42	40	45	45
3.	BMT	36	40	40	45
4.	MPG	40	43	40	45
5.	BM	32	40	46	45
6.	GD	50	50	50	50
7.	KV	40	43	43	45
8.	AA	38	38	40	43
9.	NK	45	43	45	48
10.	RS	45	50	48	50
11.	SK	40	43	45	45
12.	SS	38	40	45	50
	Mean ±S.D.	40 ±5	43 ±4	44 ±3	46 ±2

't' test : 0 : I month $p > 0.05$, I : II months $p > 0.05$
0 : II months $p < 0.05$, I : III months $p < 0.05$
0 : III months $p < 0.005$, II : III months $p > 0.05$

INTERGROUP COMPARISON

1. Comparison between tables XII and XIII reveals that the two never differed from each other at any stage ($p > 0.05$).

't' test : at 0, 1, 2 and 3 months $p > 0.05$.

2. Comparison between tables XIV and XV however, shows that initially the two groups of subjects did not differ in their HDL values ($p > 0.05$) but only after 1 month of treatment the HDL of those subjects who had initial STC 250 mg/dl or above, was significantly higher than the other subjects ($p < 0.05$) and the same significance increased at 3 months ($p < 0.005$).

't' test : 0 month $p > 0.05$
I month $p < 0.05$
II months $p < 0.05$
III months $p < 0.005$

LDL CHOLESTEROL: (TABLE XVI)

The basal LDL values of subjects receiving the hypolipidemic drug ranged from 129 mg/dl to 330 mg/dl with a mean$\pm$S.D. of 178$\pm$40 mg/dl. It fell to 160$\pm$24 mg/dl only after one month of treatment ($p < 0.05$) and again decreased more significantly to a value of 152$\pm$19 mg/dl after 2 months of therapy ($p < 0.01$). Finally a value of 147$\pm$20 mg/dl was obtained after 3 months of therapy and the difference from the basal value was highly significant ($p < 0.005$). The total fall was 17.4%.

TABLE XVI : Serum LDL cholesterol values of subjects receiving the drug C.T.I.

Sl. No.	Name	Serum LDL cholesterol (mg/dl) 0 month	1 month	2 months	3 months
1.	SAN	129	145	135	135
2.	H	203	197	180	185
3.	R	155	153	125	118
4.	RM	162	155	150	135
5.	BMT	217	205	175	165
6.	SR	167	170	150	142
7.	MPG	150	141	150	140
8.	I	157	126	135	139
9.	BM	330	101	134	125
10.	RSVP	149	130	152	150
11.	AKS	154	163	161	150
12.	SN	159	157	150	140
13.	GD	176	170	164	155
14.	KV	200	167	127	134
15.	SS	177	176	179	170
16.	AA	202	201	170	185
17.	VP	150	162	162	153
18.	RS	187	175	178	160
19.	MK	170	160	156	145
20.	SK	174	148	150	145
21.	ST	165	159	155	156
22.	SS	182	150	106	100
	Mean ±S.D.	178 ±40	160 ±24	152 ±19	147 ±20

't' test : 0 : I month $p < 0.05$
0 : II months $p < 0.01$
0 : III months $p < 0.005$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

LDL CHANGES IN DIFFERENT GROUPS

1. The starting LDL levels of those subjects having CAD as one of the complications of hypercholesterolemia ranged from 162 to 330 mg/dl with a mean of 192±56 mg/dl. It gradually decreased to 158±24 mg/dl, 158±15 and 148±15 mg/dl after 1, 2 and 3 months respectively. The last value was significantly lower than the 1st ($p < 0.05$) The total fall was 23% (Table XVII).

TABLE XVII : Serum LDL cholesterol values of subjects having CAD as one of the complications of hypercholesterolemia.

Sl. No.	Name	Serum LDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	RM	162	155	150	135
2.	SR	167	170	150	142
3.	BM	330	107	134	125
4.	GD	176	170	164	155
5.	SS	177	176	179	170
6.	RS	187	175	178	160
7.	NK	170	160	156	145
8.	ST	165	159	155	156
9.	Mean ±S.D.	192 ±56	158 ±24	158 ±15	148 ±15

't' test : 0 : I month $p > 0.05$
0 : II months $p > 0.05$
0 : III months $p < 0.05$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

2. The basal LDL of subjects not having CAD ranged from 129 to 217 mg/dl with a mean of 170±26 mg/dl. After 1 month of therapy, it fell to 160±25 mg/dl but the difference being insignificant ($p > 0.05$). Two months of treatment reduced LDL significantly to 148±21 mg/dl ($p < 0.05$) and then to 146±23 mg/dl after 3 months (Table XVIII).

TABLE XVIII : Serum LDL cholesterol values of subjects not having CAD.

Sl. No.	Name	Serum LDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	129	145	135	135
2.	H	203	197	180	185
3.	R	155	153	125	118
4.	BMT	217	205	175	165
5.	MPG	150	141	150	140
6.	I	157	126	135	139
7.	RSVP	149	130	152	150
8.	AKS	154	163	161	150
9.	SN	159	157	150	140
10.	KV	200	167	127	134
11.	AA	202	201	170	185
12.	VP	150	162	162	153
13.	SK	174	148	150	145
14.	SS	182	150	106	100
	Mean ±S.D.	170 ±26	160 ±25	148 ±21	146 ±23

't' test : 0 : I month $p > 0.05$
0 : II months $p < 0.05$
0 : III months $p < 0.05$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

3. Serum LDL cholesterol values of subjects with initial STC less than 250 mg/dl ranged from 150 to 177 mg/dl at the beginning of the study. The mean was 159±9 mg/dl. It gradually decreased to 155±16, 152±15, and 145±14 mg/dl after 1, 2 and 3 months of treatment respectively. Only the final value differed from basal value ($p < 0.05$). The total fall was 8.8% (Table XIX).

TABLE XIX : Serum LDL cholesterol changes in subjects with initial serum cholesterol between 200 to 249 mg/dl.

Sl. No.	Name	Serum LDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	R	155	153	125	118
2.	RM	162	155	150	135
3.	SR	167	170	150	142
4.	I	154	126	135	139
5.	RSVP	149	130	152	150
6.	AKS	154	163	161	150
7.	SN	159	157	150	140
8.	SS	177	176	179	170
9.	VP	150	162	162	153
10.	ST	165	159	155	156
	Mean ±S.D.	159 ± 9	155 ±16	152 ±15	145 ±14

't' test : 0 : I month $p > 0.05$
0 : II months $p > 0.05$
0 : III months $p < 0.05$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

4. Serum LDL of subjects with basal STC 250 mg/dl or more was 129 to 330 mg/dl at first with a mean of 193±49 mg/dl. It reduced to 163±30 mg/dl within 1 month ($p < 0.05$) and then decreased gradually to 152±23 and 148±24 mg/dl after 2 and 3 months respectively. The total fall was 23.3% (Table XX).

TABLE XX : Serum LDL cholesterol changes in subjects with initial serum total cholesterol 250 mg/dl or above.

Sl. No.	Name	Serum LDL cholesterol (mg/dl)			
		0 month	1 month	2 months	3 months
1.	SAN	129	145	135	135
2.	H	203	197	180	185
3.	BMT	217	205	175	165
4.	MPG	150	141	150	140
5.	BM	330	101	134	125
6.	GD	176	170	164	155
7.	KV	200	167	127	134
8.	AA	202	201	170	185
9.	RS	187	175	178	160
10.	NK	170	160	156	145
11.	SK	174	148	150	145
12.	SS	182	150	106	100
	Mean ±S.D.	193 ±49	163 ±30	152 ±23	148 ±24

't' test : 0 : I month $p > 0.05$
0 : II months $p > 0.05$
0 : III months $p < 0.05$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

INTERGROUP COMPARISON

1. Comparison between tables XVII and XVIII reveals no difference at any stage ($p > 0.05$).

't' test : at 0, 1, 2 and 3 months $p > 0.05$.

2 2. On comparing LDL values of tables XIX with table XX it was seen that initially the values were significantly higher in those subjects who had STC 250 mg/dl or higher ($p < 0.05$). But the difference was no more at 1, 2 and 3 months.

't' test : 0 month $p < 0.05$
1 month $p > 0.05$
2 months $p > 0.05$
3 months $p > 0.05$

LDL/HDL RATIO: (TABLE XXI)

The initial ratio was from 3.1 to 10.3 with a mean of 4.6 ± 1.5. Only after 1 month of treatment it came down to 3.9 ± 0.7 and the difference was highly significant ($p < 0.005$). The ratio further came down to 3.6 ± 0.6 and 3.4 ± 0.6 after 2 and 3 months respectively. There was a significant fall from 1 to 3 months as well ($p < 0.05$).

TABLE XXI : LDL/HDL ratio of subjects receiving the drug C.T.I.

Sl. No.	Name	LDL/HDL Ratio			
		0 month	1 month	2 months	3 months
1.	SAN	3.2	3.2	3.0	3.0
2.	[illegible]B	4.8	4.9	4.8	4.1
3.	R	4.4	4.4	3.1	2.8
4.	RM	5.1	4.4	4.0	3.9
5.	BMT	6.0	5.1	4.4	3.7
6.	SR	4.2	4.2	3.8	3.3
7.	MPG	3.8	3.3	3.8	3.3
8.	I	3.1	3.2	3.4	3.2
9.	BM	10.3	2.5	2.9	2.8
10.	RSVP	3.3	2.6	3.5	3.8
11.	AKS	3.8	4.0	4.0	3.4
12.	SN	4.5	4.2	3.8	3.5
13.	GD	3.5	3.4	3.3	3.1
14.	KV	5.0	3.9	3.0	3.0
15.	SS	5.1	4.6	5.1	4.2
16.	AA	5.3	5.3	4.2	4.3
17.	VP	3.8	4.0	4.0	3.8
18.	RS	4.2	4.1	4.0	3.3
19.	NK	3.8	3.2	3.2	2.9
20.	SK	4.4	3.4	3.3	3.2
21.	ST	4.1	3.7	3.9	3.9
22.	SS	4.8	3.8	2.4	2.0
	Mean ±S.D.	4.6 ±1.5	3.9 ±0.7	3.6 ±0.6	3.4 ±0.6

't' test : 0 : I month $p < 0.005$
0 : II months $p < 0.005$
0 : III months $p < 0.005$
I : II months $p > 0.05$
I : III months $p < 0.01$
II : III months $p > 0.05$

LDL/HDL CHANGES IN DIFFERENT GROUPS

1. The initial ratio in those subjects having CAD as one of the complications of hypercholesterolemia was 5.0±2.2 and it reduced to 3.8±0.7 only after 1 month ($p < 0.005$). Another one month of therapy didn't bring any change in it (3.8±0.7) and the final value was 3.4±0.5 (Table XXII).

TABLE XXII : LDL/HDL ratio of subjects having CAD as one of the complications of hypercholesterolaemia.

Sl. No.	Name	LDL/HDL Ratio			
		0 month	1 month	2 months	3 months
1.	RM	5.1	4.4	4.0	3.9
2.	SR	4.2	4.2	3.8	3.3
3.	BM	10.3	2.5	2.9	2.8
4.	GD	3.5	3.4	3.3	3.1
5.	SS	5.2	4.6	5.1	4.2
6.	RS	4.2	4.1	4.0	3.3
7.	NK	3.8	3.2	3.2	2.9
8.	ST	4.1	3.7	3.9	3.9
	Mean ±S.D.	5.0 ±2.2	3.8 ±0.7	3.8 ±0.7	3.4 ±0.5

't' test : 0 : I month $p < 0.005$
0 : II months $p < 0.005$
0 : III months $p < 0.005$
I : II months $p > 0.05$
I : III months $p > 0.05$
II : III months $p > 0.05$

2. The ratio was 4.3±0.8 in subjects not having coronary artery disease and slightly reduced to 4.0±0.8 after 1 month, the change being insignificant ($p > 0.05$). After 2 months it came down to 3.6±0.6 and the change was significant ($p < 0.05$). The final value was 3.4±0.6. It was significantly lower than the basal value ($p < 0.01$). Also there was significant fall between 1 and 3 months ($p < 0.05$) (Table XXIII).

TABLE XXIII : LDL/HDL ratio of subjects not having CAD.

Sl. No.	Name	LDL/HDL Ratio			
		0 month	1 month	2 months	3 months
1.	SAN	3.2	3.2	3.0	3.0
2.	H	4.8	4.9	4.0	4.1
3.	R	4.4	4.4	3.1	2.8
4.	BMT	6.0	5.1	4.4	3.7
5.	MPG	3.8	3.3	3.8	3.2
6.	I	3.1	3.2	3.4	3.2
7.	RSVP	3.3	2.6	3.5	3.8
8.	AKS	3.8	4.0	4.0	3.4
9.	SN	4.5	4.2	3.8	3.5
10.	KV	5.0	3.9	3.0	3.0
11.	AA	5.3	5.3	4.2	4.3
12.	VP	3.8	4.0	4.0	3.8
13.	SK	4.4	3.4	3.3	3.2
14.	SS	4.8	3.8	2.4	2.0
	Mean ±S.D.	4.3 ±0.8	4.0 ±0.8	3.6 ±0.6	3.4 ±0.6

't' test : 0 : I month $p > 0.05$
0 : II months $p < 0.05$
0 : III months $p < 0.01$
I : II months $p > 0.05$
I : III months $p < 0.05$
II : III months $p > 0.05$

3. Table XXIV shows that the basal LDL/HDL ratio in subjects with initial STC $\angle$250 mg/dl ranged from 3.1 to 5.1 with a mean of 4.1$\pm$0.7. It fell to 3.9$\pm$0.6, 3.9$\pm$5 and 3.6$\pm$0.4 after 1, 2 and 3 months of treatment respectively. Only the final and basal values differed significantly ($p \angle 0.05$).

TABLE XXIV : LDL/HDL ratio changes in subjects with initial serum cholesterol between 200-249 mg/dl.

Sl. No.	Name	LDL/HDL Ratio			
		0 month	1 month	2 months	3 months
1.	R	4.4	4.4	3.1	2.8
2.	RM	5.1	4.4	4.0	3.9
3.	SR	4.2	4.2	3.8	3.3
4.	I	3.1	3.2	3.4	3.2
5.	RSVP	3.3	2.6	3.5	3.8
6.	NKS	3.8	4.0	4.0	3.4
7.	SN	4.5	4.2	3.8	3.5
8.	SS	5.1	4.6	5.1	4.2
9.	VP	3.8	4.0	4.0	3.8
10.	ST	4.1	3.7	3.9	3.9
	Mean $\pm$S.D.	4.1 $\pm$0.7	3.9 $\pm$0.6	3.9 $\pm$0.5	3.6 $\pm$0.4

't' test : 0 : I month $p \angle 0.05$
0 : II months $p \angle 0.05$
0 : III months $p \angle 0.05$
I : II months $p \angle 0.05$
I : III months $p \angle 0.05$
II : III months $p \angle 0.05$

4. Table XXV shows LDL/HDL ratio of subjects having initial STC equal to more than 250 mg/dl. The basal ratio ranged from 3.2 to 10.3 with a mean of 4.9±1.9. It fell to 3.8±0.9 within 1 month and then gradually to 3.5±0.6 at 2 months and 3.2±0.6 after 3 months.

TABLE XXV : LDL/HDL ratio changes in subjects with initial STC 250 mg/dl or more.

Sl. No.	Name	LDL/HDL Ratio			
		0 month	1 month	2months	3 months
1.	SAN	3.2	3.2	3.0	3.0
2.	H	4.8	4.9	4.0	4.1
3.	BMT	6.0	5.1	4.4	3.7
4.	MPG	3.8	3.3	3.8	3.1
5.	BN	10.3	2.5	2.9	2.8
6.	GD	3.5	3.4	3.3	3.1
7.	KV	5.0	3.9	3.0	3.0
8.	AA	5.3	5.3	4.2	4.3
9.	RS	4.2	4.1	4.0	3.3
10.	NK	3.8	3.2	3.2	2.9
11.	SK	4.4	3.4	3.3	3.2
12.	SS	4.8	3.8	2.4	2.0
	Mean ±S.D.	4.9 ±1.9	3.8 ±0.9	3.5 ±0.6	3.2 ±0.6

't' test : 0:I month $p < 0.05$, I : II months $p > 0.05$
0:II months $p < 0.05$ I : III months $p < 0.05$
0:III months $p < 0.05$ II : III months $p > 0.05$

INTERGROUP COMPARISON

1. On compering the tables XXII with XXIII it was found that they didn't differe from each other at any time ($p > 0.05$).

't' test : at 0, 1, 2 and 3 months $p > 0.05$.

2. Similarly, comparison of table XXIV with table XXV reveals that there was no difference between the groups.

't' test :	0 month 1 month 2 months 3 months	p 70.05

SIDE EFFECTS

Table XXVI elaborates the various side effects reported by the subjects at different times of the trial.

TABLE XXVI : Showing the side effects of the drug.

Sl. No.	Name	Side effect	Result
1.	AKS	Gastritis	Dropped after 1 month
2.	KND	Gastritis	Dropped after 1 month
3.	BM	Gastritis	Subsided after continuing treatment.
4.	RSVP	Frequent motions	Continued treatment.
5.	MPG	Gastritis	Dropped after 1 week.
6.	SN	Day time drowsiness	Continued treatment and decreased.
7.	GD	Frequent motions	Continued treatment and decreased.
8.	RS	Gastritis	Dropped after 2 weeks.
9.	RP	Gastritis	Dropped after 1 month
10.	RS	Gastritis	Continued treatment.
11.	SS	Gastritis	Continued treatment.

The table XXVI shows that out of 30 subjects 8(26.7%) reported gastritis and 5 of them had to stop taking the drug. The symptoms din't subside after continued treatment. Out of total 8 dropped cases at various intervals, these 5 (62.5%) subjects dropped on account of side effects. Two (6.7%) subjects reported increased frequency of stools, but the same subsided itself after continued treatment.

Another subject (3.3%) complained of increased day time drowsiness which however, was not distressing and subsided after contunuing the treatment.

Apart from the mentioned side effects we did not observe any adverse effect on liver or renal function tests nor did we observe any change in hematological parameters.

D I S C U S S I O N

DISCUSSION

Myocardial infarction is a global problem. One of the major risk factor for myocardial infarction is hyperlipidemia (hyperlipoproteinemia) leading to atherosclerosis. Medical scientists are of the opinion that antilipidemic, antidiabetic and antihypertensive drugs and other measures that can decrease catecholamine levels are considered to be remedy for myocardial infarction(Haab,1971). It is now a well established fact that reduction in blood cholesterol levels reduces the risk of myocardial ischemia. 25% reduction of blood cholesterol levels reduced the risk of myocardial ischemia by 50% (Lowering blood cholesterol 1985, Tyroler, 1987). Vigorous global research is going on to search the agents to control hyperlipidemia. Indian scientists have directed their research towards herbs having hypolipidemic and cardioprotective potential based on few references in age old Ayurvedic texts (Satyavati, 1966).

The vast research based data accumulated so far indicates that Terminalia arjuna W & A has cardiotonic and stimulant action on heart (Ghoshal, 1909). At the same time it proved to possess diuretic activity (Caius et al, 1930), decreased the blood pressure (Singh et al, 1982), prolonged prothrombin time (Chaturvedi, 1973), had PGE_2 like activity (Dwivedi et al, 1987), hypolipidemic and hypoglycaemic activity (Dwivedi et al, 1988).

On clinical trials Terminalia arjuna was found to be diuretic (Caius et al, 1930). It has observed to be effective in congestive heart failure, essential hypertension and cirrhosis of liver (Colabawalla, 1981). Chaturvedi (1973) found it to be beneficial in the patients of ischaemic heart disease. In one patient of complete heart block T. arjuna helped the heart rate to return to sinus rhythm (Udupa et al, 1986). Dwivedi et al found it to be effective modifier of risk factors of myocardial infarction and it appeared to be cardioprotective.

Inula racemosa Hook blocked hypertensive response of Histamine and 5 HT (Singh et al, 1980), had negative inotropic and negative chronotopic effects on frog heart (Sharma et al, 1986), and possessed cardioprotective, hypoglycaemic and hypocholesterolemic activities (Dwivedi et al, 1988). It prevented post exercise ST segment depression in patients of ischaemic heart disease. The results were comparable with nitroglycerine (Tripathi et al, 1984a). It also reduces number of episodes of angina pectoris (Dwivedi et al, 1989).

Gum resin of commiphora mukul (Guggulu) has been subjected to vigorous investigations and experimentations for past two decades. It was found to possess potent hypolipidemic activity (Tripathi et al, 1967). Clinical studies have been performed on the large number of patients of ischaemic heart disease coronary insufficiency and

other lipid disorders. It was found to be effective modifier of risk factors for myocardial infarction. Hypolipidemic activity was well comparable to clofibrate (Malhotra et al, 1977; Tripathi et al, 1968; Satyavati, et al, 1966).

Combination of Pushkarmoola and Guggulu proved to be very effective modifier of coronary risk factor (Tripathi et al, 1984a). Hence a combination of Terminalia arjuna W & A, Inula racemosa Hook and Gum resin of commiphora mukul Hook ex stocks was thought to be most suitable cardioprotective, antianginal and hypolipidemic formulation on the basis of :

- Antianginal, hypoglycaemic and hypolipidemic activities of Inula racemosa Hook.
- Cardioprotective, cardiotonic, hypoglycaemic and hypolipidemic actions of Terminalia arjuna W & A.
- Hypocholesterolemic, hypotriglyceridemic, LDL lowering and HDL raising properties of Gum resin of commiphora mukul.

But since the combination has been made for the first time, it needed clinical trials in volunteers before making it available in the market. Hence it was felt desirable to conduct the present study on human volunteers with elevated serum cholesterol levels to know :

1. The efficacy of the drug on lipid profile.
2. The side effects of the drug.

EFFECTIVENESS OF THE DRUG

In our present study, we have examined the effect of the drug on various components of the lipid in the serum as follows :

Serum Total Cholesterol (STC)

The serum total cholesterol fall observed by us was 11.2% and thus it is comparable with clofibrate, Gemfibrozil and probucol which reduce STC by 6-11%, 11% and 10-15% respectively.

The maximum reduction occurred in the first month (6.9%). A fall of 15.3% was observed in subjects having coronary artery disease, but it was not statistically significant. There are two reasons for it: 1. The group is too small and (2) The variability of the initial STC (S.D. - 67) is large.

Whereas, in case of subjects not having CAD, though the observed fall in STC is only 9.1%, but it is statistically significant. The idea is further supported by the intergroup comparison which shows that no difference existed between the two groups at any time.

The overall reduction in STC was only 11.2% in our study, whereas previous studies on Commiphora mukul have reported greater reduction. Malhotra et al (1971) reported 27% fall by giving 1.0 gm per day of fraction A for 6-34 weeks. In another study he achieved 26% fall by giving 1.5 g/day of fraction A for 75 weeks. Upadhyay

et al (1976) observed a fall by 27.8% whereas Tripathi et al (1976) reported 24.5% fall. In a similar study, Malhotra et al (1977) reported 36.8% reduction in STC whereas Gupta et al (1978) observed 35.8% fall.

In another study, there was a reduction in STC of 27% (Upadhyay et al, 1982) and 27.4% (Agarwal et al, 1986). In the multicentric clinical trials carried out with gugulipid in primary hyperlipidaemic cases at 7 different centres in India coordinated and in collaboration with the Central Drug Research Institute, Lucknow, the average fall in cholesterol was 21.59% in the open trials and 12.6% in double blind cross over trial, the range being 5.6 to 26.8%.

Our results are comparable with those of Saxena (1980) and Agarwal et al (1986) who observed a decrease in serum cholesterol by 15% and 16.9% respectively. Similarly, Tripathi et al (1984) reported 17.4% reduction by using a combination of Guggulu and Pushkarmula.

The underlying cause for a lower observed reduction in our study may be two folds :

1. The dose of C. mukul used by us was too small(2.0 g/day for 12 weeks), whereas other researchers usually gave it in a dose of 6 to 16 g/day, or used the fraction A of C. mukul.
2. The initial STC of subjects was not so high in present study, whereas the drug is more effective when the

basal cholesterol values were high. The fact is supported by our observations that the STC levels did not reduce significantly in those persons who had initial STC less than 250 mg/dl, whereas it was highly significant in those with basal STC 250 mg/dl or above. Intergroup comparison further supports the idea : there is difference between two groups only upto one month.

Triglycerides (STG)

Tiwari et al (1990) and Pathak et al (1990) reported triglyceride lowering effect of T. arjuna. In a study, clinical efficacy of fraction A of gum guggulu as hypolipidaemic agent was evaluated in comparison to ethyl-p-chlorophenoxy isobutyrate and CIBA-13437-Su. Fraction A of gum guggulu was administered in the dose of 1.0 g in two divided doses daily. The duration of treatment varied from 6 to 34 weeks. Statistical analysis revealed that fraction A triglycerides lowered significantly the serum triglycerides besides lowering other lipid fractions and the lowering of triglycerides was found most encouraging in case of gum guggulu in comparison to all the known drugs (Malhotra et al, 1971). Similarly the other workers have noted a triglyceride lowering effect of C. mukul(Malhotra et al, 1977; Upadhyay et al, 1976; Gupta et al, 1978; Saxena, 1980; Agarwal et al, 1986; Upadhyay et al, 1982; Kotiyal et al, 1984; Tripathi et al, 1984). In our present study,

we did not observe any change in serum triglyceride in any group of subjects.

HDL Cholesterol

We have observed a rise in HDL of 10% after 3 months of therapy. Thus the efficacy of the drug is comparable to lovastatin and Gemfibrozil which raise the HDL by 10-13% and 10-25% respectively. Half of this rise occurred in 1st month and remaining in the last month. Group-wise, subjects with CAD has 10% rise in HDL but it come to be statistically insignificant again because :

1. The group was too small and
2. The standard deviation was too large. The fact is supported by the finding that there is no intergroup difference statistically at any stage. The subjects without having CAD also recorded 10% rise in HDL and it was statistically significant.

However, those who had initial STC less than 250 mg/dl did not show any significant increase in HDL (total rise only 5%) whereas it significantly increased in subjects with basal STC 250 mg/dl or above. Intergroup comparison also supports this fact that though the initial HDL levels were similar in two groups, it was higher in the latter group after 1 month of therapy and significantly so after 3 months. In the previous studies, only Tiwari et al (1990) and Pathak et al (1990) have reported HDL

raising properties of Terminalia arjuna and our findings support this view. In the multicentric clinical trials on gugulipid in a dose of 500 mg TDS for 12 weeks, conducted by CDRI, Lucknow, an HDL increase of 13.3%, 30.1%, 6.4% and 20.4% was reported from Bombay, Jaipur (a & b) and Lucknow respectively. The average increase was 16.07%.

LDL Cholesterol

In this study, we have observed a definite fall of 17.4% in serum LDL cholesterol. The maximum fall of 10% was observed during the first month. Of the currently available drugs, Lovastatin reduces LDL by 20-40% Gemfibrozil by 10%, bile acid binding resins by 20% and Nicotinic acid by 10-15%, Probucol reduces it by less than 10%.

In subjects with coronary artery disease a total LDL fall of 23% was observed. The maximum fall of 17.7% occurred in first month. Whereas in those without coronary artery disease it was only 14% in 3 months. Though the groups did not differ much statistically at any time, the greater fall in LDL is of course beneficial to patients of coronary artery disease.

In the other two groups, the LDL cholesterol fell by only 8.8% in those subjects who had initial serum cholesterol less than 250 mg/dl whereas the same was 23.3% in those with STC $\geq$250 mg/dl. Intergroup comparison confirms this finding i.e. the LDL cholesterol values differed at

the beginning of the treatment but the values were no more different after one month. It means that the drug brings LDL to normal, whatever the initial value may be, that is, to say, the greater the initial LDL value, the greater is the efficacy of the drug.

In the multicentric clinical trials conducted by CDRI, Lucknow, LDL cholesterol estimation was carried out at Bombay, Jaipur and Lucknow only and it was significantly lowered in those cases who responded to gugulipid therapy. A total fall of 14.11%, 22.34%, 8.84% and 16.31% was reported from Bombay, Jaipur(a & b) and Lucknow respectively, the average fall being 16.74%, which is quite close to our results.

LDL/HDL Ratio

In our study, the LDL/HDL ratio fell significantly from 4.6 ± 1.5 to 3.4 ± 0.6 ($p < 0.05$) and the maximum effect was found in the first month. The fall was more significant in persons with coronary artery disease ($p < 0.005$) than in the other groups ($p < 0.001$). The effect may be beneficial to patients of CAD. Similarly, the fall is more significant in subjects with initial serum cholesterol greater than 250 mg/dl ($p < 0.001$) than in those who had basal STC less than that ($p < 0.05$). However, the effect of CAD or basal STC is not seen in intergroup comparison.

A significant decrease was also reported by multicentric clinical trials on gugulipid carried out by CDRI, Lucknow.

Thus we have found the combination to be effective in lowering serum cholesterol, LDL cholesterol and LDL/HDL ratio and raising HDL cholesterol. In the present study the data of responders and non-responders have been dubbed together and the pooled data analysed by paired 't' test for statistical significance, while in previous reports, the effects have been considered in responders only. Had we also done the same, our results would have been much better than this. Besides, we have permitted our subjects their usual life style, which could have a major bearing on the results.

SIDE EFFECTS

We have observed gastritis in 26.7%, increased frequency of motions in 6.7% and drowsiness in 3.3% cases, the total being 36.7%, which is very high and the former was quite distressing to the subjects resulting in high drop out rate and poor compliance.

In previous studies, except mild diarrhoea in 5 cases out of 41 cases no other side effects were observed with guggulu (Malhotra et al, 1977) that too with fraction A in the dose of 1.5 g/day for 75 weeks. The same author had reported hiccough in one patient, diarrhoea in three patients and restlessness and apprehension in one patient

in 1971 by using fraction A of gum guggulu in a dose of 1.0 g/day.

Agarwal et al (1986) used guggulipid in a dose of 1.2 g/day in their study. The aim of the study was to evaluate the safety of the drug on long term administration to human beings. The drug was found to be completely safe and did not produce any alteration in hepatic or renal functions, blood sugar levels, hematological parameters and electrocardiogram. Similar findings have been confirmed by us in the present study.

In the multicentric clinical trials by CDRI, Lucknow, only one patient out of two hundred and five patients studied showed gastrointestinal symptoms which did not necessitate withdrawal of the drug. Otherwise, it was found to be completely devoid of any effect on liver function, blood sugar and blood urea levels, hematological parameters and electrocardiogram.

SUMMARY & CONCLUSION

SUMMARY AND CONCLUSIONS

The present study was carried out on 30 subjects of hyperlipidemia. Out of which, 22 completed the three months trials. Of the latter, 8 subjects were having coronary artery disease and 12 were having basal serum cholesterol 250 mg/dl or greater. The subjects were given a drug containing C. mukul, T. arjuna and I. racemosa 500 mg each in capsule form in a dose of 2 B.D. for 3 months and monthly lipid profile was done and subjects assessed for any side effects. Serum cholesterol fell significantly from 259±43 to 230±16 mg/dl ($p < 0.005$). Triglycerides showed no significant change ($p > 0.05$) while HDL cholesterol rose significantly from 40±5 to 44±4 mg/dl ($p < 0.005$). LDL cholesterol fell from 178±40 to 147±20 mg/dl ($p < 0.005$). LDL/HDL ratio decreased from 4.6±1.5 to 3.4±0.6 ($p < 0.005$). Out of 8 dropped cases 5 had severe gastritis, while rest of 3 dropped without reason.

On the basis of observations we conclude that :

1. The drug effectively lowers serum cholesterol and LDL cholesterol and raises HDL cholesterol, thereby reduces the LDL/HDL ratio as well.
2. The maximum effect is observed in the first month of treatment.
3. High the initial serum cholesterol level, greater is the efficacy of the drug.

4. The drug is equally effective in healthy and diseased persons.

5. The main side effect is gastritis and may need withdrawal of the drug.

6. It has no effect on liver, kidneys or any haematological parameters.

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A P P E N D I X

APPENDIX - I

WORKING PROFORMA

CLINICAL TRIALS ON HYPOLIPIDAEMIC/CARDIOPROTECTIVE DRUG

Case No. _____

OPD/MRD No. _____ Dated:

Name :

Age/Sex :

Address :

Religion :

Occupation :

Socio-economic Status:

Physical Activity : Sedentary/Active/Very Active

Any emotional/mental stress in life :

- -

CHIEF COMPLAINTS

PAST HISTORY(Any CAD/MI/STROKE etc.).

CONCOMITANT ILLNESSES(Diabetes mellitus/Nephrotic syndrome/Cirrhosis of liver etc.)

FAMILY HISTORY

TREATMENT HISTORY

PERSONAL HISTORY

Weekly / monthly consumption of

Type of food	Before Drug therapy	During Drug therapy	[illegible]
Ghee			
Oils			
Milk/Cheese etc.			
Eggs			
Meat/Chicken fish			
Smoking			
Alcohol			
Tobacco			
Contraceptives			
Others			

CLINICAL ASSESSMENT

I. SUBJECTIVE

Parameters	Initial	During therapy			[illegible]
	0	1	2	3	
Appetite					
Sleep					
Motions					
Activity					
General					
Feeling					
Libido					
Sex life					

II. OBJECTIVE Height (cm) :

Parameters	Initial 0	During therapy 1	2	3
Pulse Rate				
B.P.				
Resp. Rate				
Temperature				
Weight (kg)				
Icterus				
Pallor				
Cyanosis				
Clubbing				
Oedema				
Hydration				
Lymph Nodes				
JVP				
Organomegaly				
Xanthomas				
Others				

LABORATORY ASSESSMENT

1. ROUTINE INVESTIGATIONS

Parameters	Initial 0	During therapy 1	2	3
BLOOD				
TLC				
DLC : P				
L				
E				
M				
B				
Hb				
ESR				
Blood Urea				
Sr.Creatinine				
Blood Sugar				
F				
PP				
R				
LFT : SGOT				
SGPT				
Alk.Phos.				
URINE : Alb.				
Sugar				
M/E				
E.C.G.				
X-ray Chest				
Others				

III. LIPID PROFILE

Parameters	Initial 0	During therapy 1	2	3
Total cholesterol				
Total Triglycerides				
HDL Cholesterol				
VLDL-c (Calculated)				
LDL-c (Calculated)				

Impression :

Signature of Investigator:

MASTER CHART - I

General characteristics of subjects receiving hypolipidaemic drug (C.T.I.).

Sl. No.	Name	Age/ Sex	Weight (kg)	Height (cms)	Diagnosis	Family history
1.	AKS	38/M	78	170.0	Healthy	Mother - hypertensive Father - Myocardial infarction
2.	SAN	35/M	65	155.0	Healthy	Father - hypertensive
3.	H	35/F	67	145.0	Healthy	No
4.	R	32/M	65	160.0	Healthy	Father - hypertensive
5.	KND	65/M	64	162.5	C.A.D.	No
6.	RM	48/F	65	152.5	CAD with mild hyper-tension	No
7.	BMT	50/M	58	150.0	Healthy	No
8.	SR	28/M	72	167.5	C.A.D.	No
9.	MPG	56/M	72	165.0	Healthy	No
10.	I	29/F	64	150.0	Healthy	Father - M.I. Mother - hypertensive & diabetic
11.	BKY	55/M	68	162.5	Healthy	No
12.	BM	54/M	86	170.0	CAD + Hypertension	No
13.	RSVP	43/M	68	162.5	Healthy	Father - Diabetic, hyper-tension,& CVA.
14.	MPG	36/M	60	157.5	Mild hypertension	No
15.	AKS	41/M	66	162.5	Diabetes + Hyper-tension	Father - Diabetic and hypertensive

Contd. ...

Contd. ...

16.	SN	36/M	66	160.0	Diabetes mellitus	Mother - hypertensive
17.	GD	45/F	70	162.5	IHD with hypertension	Father - DM + hypertension
18.	KV	55/M	70	170.0	Hypertension	No
19.	SS	50/M	61	165.0	I.H.D.	Father - hypertensive Mother - hypertensive
20.	RS	59/M	52	160.0	I.H.D.	No
21.	RP	62/M	68	170.0	Diabetes mellitus	Father - Diabetes mellitus Mother - Hypertensive
22.	AA	36/F	63	155.0	Healthy	No
23.	VP	60/M	62	167.5	Healthy	Father - Diabetes mellitus + hypertensive
24.	RS	45/M	65	167.5	I.H.D.	Father - M.I.
25.	NK	58/M	71	160.0	DM + IHD + hypertension	No
26.	SK	52/F	56	150.0	Healthy	No
27.	MK	43/M	66	162.5	I.H.D.	Father - C.A.D. Mother - Diabetes mellitus
28.	ST	31/M	58	165.0	C.A.D.	No
29.	UR	38/F	60	152.5	Diabetes mellitus	Father - hypertensive
30.	SS	40/F	67	150.0	Healthy	No
	Mean ±S.D.	45 ±10	66 ±6	160.3 ± 7.0		

Sl. No.	Smoking	Alcohol	Weekly consumption of				
			Ghee (kg)	Milk (l)	Oils (l)	Eggs (No.)	Meat (kg)
1.	No	No	0.12	3.5	0.25	7	No
2.	No	No	No	No	0.25	No	NO
3.	No	No	0.05	No	0.12	3	0.15
4.	No	No	0.60	4.0	No	7	No
5.	No	No	0.25	3.5	No	7	No
6.	No	No	No	2.1	0.40	No	No
7.	No	No	0.20	4.2	0.20	No	No
8.	Yes	No	0.75	5.0	No	14	0.20
9.	No	No	0.25	2.1	No	No	No
10.	No	No	0.25	2.5	0.25	No	No
11.	No	Yes	No	1.7	0.50	14	0.50
12.	Yes	Yes	No	2.1	0.12	3	0.50
13.	No	No	No	4.0	0.25	No	No
14.	No	No	0.50	2.5	No	7	No
15.	No	No	No	2.0	0.25	7	0.20
16.	No	No	No	2.0	0.25	No	No
17.	No	No	0.50	4.0	No	No	No
18.	Yes	No	No	3.0	0.30	7	No
19.	No	No	No	3.0	0.25	No	No
20.	No	No	0.50	2.0	No	No	No
21.	Yes	No	No	3.0	0.40	14	0.50
22.	No	No	1.00	3.0	No	No	No
23.	Yes	Yes	No	3.0	0.25	7	0.20
24.	No	Yes	0.25	2.0	0.25	14	0.20
25.	No	No	No	3.0	0.50	No	No
26.	No	No	0.50	2.0	0.25	No	No
27.	Yes	Yes	No	2.0	0.50	No	No
28.	No	No	0.50	2.5	No	7	No
29.	No	No	0.25	3.5	0.25	7	No
30.	No	No	0.75	3.0	No	No	No

MASTER CHART - II

Lipid profile of subjects receiving hypolipidaemic drug C.T.I.

Sl. No.	Name	Serum Cholesterol(mg%)				Serum Triglyceride(mg%)			
		0 month	1month	2months	3 months	0 month	1 month	2 months	3 months
1.	AKS	270	260	D	-	300	390	D	-
2.	SAN	265	250	250	240	480	300	350	300
3.	H	267	260	255	250	110	115	150	100
4.	R	230	228	215	200	200	200	250	200
5.	KND	237	235	D	-	180	180	D	-
6.	RM	228	220	220	200	172	150	160	150
7.	BMT	292	283	270	250	195	190	225	200
8.	SR	243	250	230	225	186	200	200	200
9.	MPG	250	232	240	230	300	240	250	225
10.	I	245	196	205	214	190	154	150	162
11.	BKY	214	D	-	-	142	D	-	-
12.	BM	430	201	238	222	340	300	292	260
13.	RSVP	230	225	245	240	180	225	250	250
14.	MPG	250	D	-	-	250	D	-	-
15.	AKS	235	244	240	238	203	200	196	218

Contd. ...

Contd. .....

16.	SN	226	230	220	210	160	180	150	150
17.	GD	250	240	240	230	120	100	130	125
18.	KV	280	250	210	215	200	200	200	180
19.	SS	240	250	250	250	140	180	180	200
20.	RS	220	D	-	-	100	D	-	-
21.	RP	255	250	D	-	160	170	D	-
22.	AA	280	275	250	260	200	180	200	160
23.	VP	230	250	250	240	200	240	240	235
24.	RS	260	250	255	240	140	160	160	160
25.	NK	265	250	240	225	250	200	180	150
26.	SK	260	235	240	230	230	220	225	200
27.	MK	240	235	D	-	140	160	D	-
28.	ST	225	230	225	225	100	140	150	145
29.	UR	235	240	250	D	150	145	160	D
30.	SS	270	250	215	220	250	300	320	350
	Mean	254	241	237	230	199	201	207	196
	±S.D.	±38	±19	±17	±16	±78	±63	±58	±58

D = Dropped

Contd. ....

Sl. No.	HDL Cholesterol (mg%)				LDL Cholesterol (mg%)				LDL/HDL Ratio			
	0 month	1 month	2 months	3 months	0 month	1 month	2 months	3 months	0 month	1 month	2 months	3 months
1.	50	54	D	-	160	128	D	-	3.2	2.4	D	-
2.	40	45	45	45	129	145	135	135	3.2	3.2	3.0	3.0
3.	42	40	45	45	203	197	180	185	4.8	4.9	4.0	4.1
4.	35	35	40	42	155	153	125	118	4.4	4.4	3.1	2.8
5.	43	40	D	-	158	159	D	-	3.7	4.0	D	-
6.	32	35	38	35	162	155	150	135	5.1	4.4	4.0	3.9
7.	36	40	40	45	217	205	175	165	6.0	5.1	4.4	3.7
8.	40	40	40	43	167	170	150	142	4.2	4.2	3.8	3.3
9.	40	43	40	45	150	141	150	140	3.8	3.3	3.8	3.1
10.	50	39	40	43	157	126	135	139	3.1	3.2	3.4	3.2
11.	42	D	-	-	144	D	-	-	3.4	D	-	-
12.	32	40	46	45	330	101	134	125	10.3	2.5	2.9	2.8
13.	45	50	43	40	149	130	152	150	3.3	2.6	3.5	3.8
14.	40	D	-	-	160	D	-	-	4.0	D	-	-
15.	40	41	40	44	154	163	161	150	3.8	4.0	4.0	3.4

Contd. .....

16.	35	37	40	40	159	157	150	140	4.5	4.2	3.8	3.5
17.	50	50	50	50	176	170	164	155	3.5	3.4	3.3	3.1
18.	40	43	43	45	200	167	127	134	5.0	3.9	3.0	3.0
19.	35	38	35	40	177	176	179	170	5.1	4.6	5.1	4.2
20.	40	D	-	-	160	D	-	-	4.0	D	-	-
21.	43	45	D	-	180	171	D	-	4.2	3.8	D	-
22.	38	38	40	43	202	201	170	185	5.3	5.3	4.2	4.3
23.	40	40	40	40	150	162	162	153	3.8	4.0	4.0	3.8
24.	45	43	45	48	187	175	178	160	4.2	4.1	4.0	3.3
25.	45	50	48	50	170	160	156	145	3.8	3.2	3.2	2.9
26.	40	43	45	45	174	148	150	145	4.4	3.4	3.3	3.2
27.	50	48	D	-	162	155	D	-	3.2	3.2	D	-
28.	40	43	40	40	165	159	155	156	4.1	3.7	3.9	3.9
29.	50	48	45	D	155	163	173	D	3.1	3.4	3.8	D
30.	38	40	45	50	182	150	106	100	4.8	3.8	2.4	2.0
Mean ±S.D.	41 ±5	42 ±5	42 ±4	44 ±4	173 ±35	159 ±23	153 ±19	147 ±20	4.3 ±1.3	3.8 ±0.7	3.6 ±0.6	3.4 ±0.6